(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 April 2003 (03.04.2003)

PCT

(10) International Publication Number
WO 03/026590 A2

(51) International Patent Classification[7]: A61K

(21) International Application Number: PCT/US02/31091

(22) International Filing Date:
27 September 2002 (27.09.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/325,664 28 September 2001 (28.09.2001) US

(71) Applicant: **BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM** [US/US]; 201 West 7th Street, Austin, TX 78701 (US).

(72) Inventors: **BELCHER, Angela, M.**; 35 Balfour Street, Lexington, MA 02421 (US). **SMALLEY, Richard, E.**; Rice University, Space Science Bldg, Room 301a, 6100 Main Street, Houston, TX 77005-1892 (US). **RYAN, Esther**; 11653 Cherryview Lane, San Jose, CA 95116 (US). **LEE, Seung-Wuk**; Rice University, Space Science Bldg, Room 301a, 6100 Main Street, Houston, TX 77005-1892 (US).

(74) Agents: **WARREN, Sanford, E., Jr.** et al.; Gardere Wynne Sewell LLP, Suite 3000, 1601 Elm Street, Dallas, TX 75201-4761 (US).

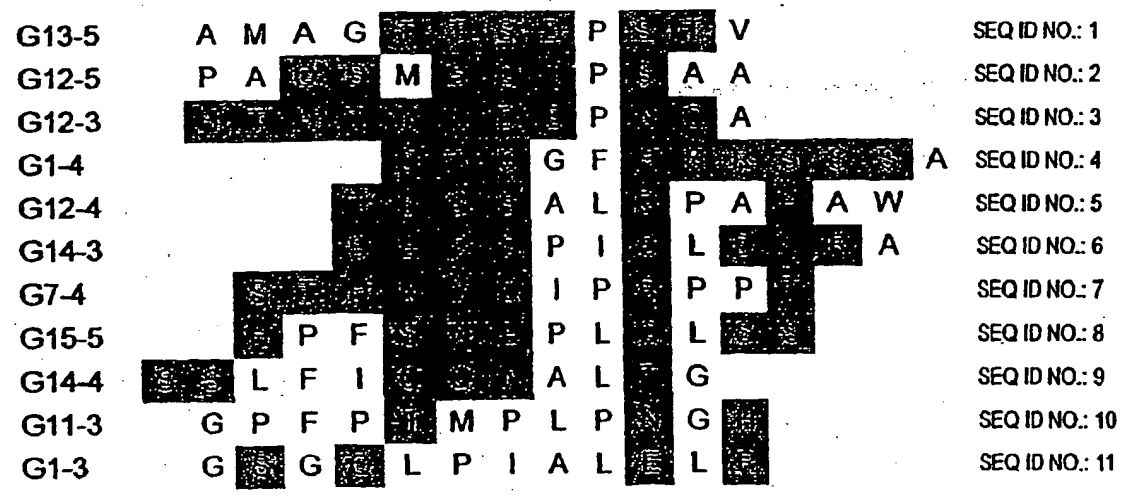
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

[Continued on next page]

(54) Title: BIOLOGICAL CONTROL OF NANOPARTICLES



(57) Abstract: The present invention includes compositions and methods for selective binding of amino acid oligomers to semiconductor and elemental carbon-containing materials. One form of the present invention is a method for controlling the particle size of the semiconductor or elemental carbon-containing material by interacting an amino acid oligomer that specifically binds the material with solutions that can result in the formation of the material. The same method can be used to control the aspect ratio of the nanocrystal particles of the semiconductor material. Another form of the present invention is a method to create nanowires from the semiconductor or elemental carbon-containing material. Yet another form of the present invention is a biologic scaffold comprising a substrate capable of binding one or more biologic materials, one or more biologic materials attached to the substrate, and one or more elemental carbon-containing molecules attached to one or more biologic materials.

WO 03/026590 A2

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

BIOLOGICAL CONTROL OF NANOPARTICLES

FIELD OF THE INVENTION

The present invention is directed to the selective recognition of various materials in general and, specifically, toward surface recognition of semiconductor materials and elemental carbon-containing materials using organic polymers.

This application claims priority from Provisional Patent Application Serial No. 60/325,664, filed on September 28, 2001.

The research carried out in the subject application was supported in part by grants from the Army Research Office (DADD19-99-0155).

A nucleotide and/or amino acid sequence listing is incorporated by reference of the material on computer readable form.

BACKGROUND OF THE INVENTION

In biologic systems, organic molecules exhibit a remarkable level of control over the nucleation and mineral phase of inorganic materials such as calcium carbonate and silica, and over the assembly of crystallites and other nanoscale building blocks into complex structures required for biologic function. This control could, in theory, be applied to materials with interesting magnetic, electrical or optical properties.

Materials produced by biologic processes are typically soft, and consist of a surprisingly simple collection of molecular building blocks (i.e., lipids, peptides, and

nucleic acids) arranged in astoundingly complex architectures. Unlike the semiconductor industry, which relies on a serial lithographic processing approach for constructing the smallest features on an integrated circuit, living organisms execute their architectural "blueprints" using both covalent and non-covalent forces acting simultaneously upon many molecular components. Furthermore, these structures can often elegantly rearrange between two or more usable forms without changing any of the molecular constituents.

The use of "biologic" materials to process the next generation of microelectronic, optic and magnetic devices provides a possible solution to resolving the limitations of traditional processing methods. The critical factors in this approach are identifying the appropriate compatibilities and combinations of biologic-inorganic-organic materials, the synthetic process and recognition for creating unique and specific combinations, and the understanding the synthesis of the appropriate building blocks.

SUMMARY OF THE INVENTION

The present invention is based on the selection, production, isolation and characterization of organic polymers, e.g., peptides, with enhanced selectivity to various organic and inorganic materials. In one embodiment of the present invention, biologic materials, e.g., combinatorial libraries such as a phage display library, cause directed molecular recognition of a target taking advantage of iterative rounds of peptide evolution. Organic polymers (e.g., peptides) may be created and derived that attach with high specificity to a wide range of materials including but not limited to semiconductor surfaces and elemental carbon-containing compounds such as carbon

nanotubes and graphite. Furthermore, the invention allows for the selective isolation of organic recognition molecules (e.g., organic polymers) that may specifically recognize a specific orientation, shape or structure of the biologic material (e.g., crystallographic shape or orientation), whether or not a composition of the structurally similar material is used.

In one embodiment of the present invention, a biologic scaffold is disclosed. The scaffold includes a substrate capable of binding one or more biologic materials, one or more biologic materials attached to the substrate, and one or more elemental carbon-containing molecules attached to the biologic materials. In another embodiment of the present invention, a biologic scaffold is disclosed that includes a substrate capable of binding one or more biologic materials, a first biologic material attached to the substrate and a second biologic material attached to the first biologic material, and one or more elemental carbon-containing molecules attached to the second biologic material.

In another embodiment of the present invention, the biologic scaffold includes a substrate capable of binding one or more bacteriophages, one or more bacteriophages attached to the substrate, one or more peptides that recognize a portion of the bacteriophage, and one or more elemental carbon-containing molecules that recognize the peptide.

In another embodiment of the present invention, a method of making a biologic scaffold is disclosed. The method includes providing a substrate capable of binding one or more biologic materials, attaching one or more biologic materials to the substrate, and contacting one or more elemental

carbon-containing molecules with the biologic material to form a biologic scaffold.

In another embodiment of the present invention, a molecule is described. The molecule contains an organic polymer that selectively recognizes an elemental carbon-containing molecule.

In another embodiment of the present invention, a method for directed semiconductor formation is described. The method includes the steps of contacting a molecule that binds a predetermined face specificity semiconductor material with a first ion to create a semiconductor material precursor and adding a second ion to the semiconductor material precursor, wherein the molecule directs formation of the predetermined face specific semiconductor material. The molecule may include an amino acid oligomer or peptide, which may be on the surface of a bacteriophage as part of, e.g., a chimeric coat protein. The molecule may even be a nucleic acid oligomer and may be selected from a combinatorial library. The molecule may be an amino acid polymer of between about 7 and 20 amino acids. The present invention also encompasses a semiconductor material made using the method of the present invention.

Uses for the controlled crystals directed and grown using the materials and methods of the present invention include materials with novel optical, electronic and magnetic properties. As will be known to those of skill in the art, the detailed optical, electronic and magnetic properties may be directed by the formation of semiconductor crystal by, e.g., patterning the devices, which using the present invention may include layering or laying down patterns to create crystal formation in patterns, layers or even both.

Another use of the patterns and/or layers formed using the present invention is the formation of semiconductor devices for high density magnetic storage. Another design may be for the formation of transistors for use in, e.g., quantum computing. Yet another use for the patterns, designs and novel materials made with the present invention include imaging and imaging contrast agent for medical applications.

One such use for the directed formation of semiconductors and semiconductor crystals and designs include information storage based on quantum dot patterns, e.g., identification of friend or foe in military or even personnel situations. The quantum dots could be used to identify individual soldiers or personnel using identification in fabric, in armor or on the person. Alternatively, the dots may be used in coding the fabric of money. Yet another use for the present invention is to create bi and multi-functional peptides for drug delivery in trapping the drug to be delivered using the peptides of the present invention. Yet another use is for in vivo and vitro diagnostics based on gene or protein expression by drug trapping using the peptides to deliver a drug.

For a more complete understanding of the features and advantages of the present invention, reference is now made to the detailed description of the invention along with the accompanying figures.

BRIEF DESCRIPTION OF THE FIGURES

For more complete understanding of the features and advantages of the present invention, reference is now made to the detailed description of the invention along with the accompanying FIGURES.

FIGURE 1 depicts selected random amino acid sequences in accordance with the present invention;

FIGURE 2 depicts XPS spectra of structures in accordance with the present invention;

FIGURE 3 depicts phage recognition of heterostructures in accordance with the present invention;

FIGURES 4-8 depict specific amino acid sequences in accordance with the present invention;

FIGURE 9 depicts the peptide insert structure of the phage libraries in accordance with the present invention;

FIGURE 10 depicts the various amino acid substitutions in the third and fourth rounds of selection in accordance with the present invention;

FIGURE 11 depicts the amino acid substitutions after the fifth round of selection in accordance with the present invention;

FIGURE 12 depicts the nanowire made from the ZnS nanoparticles in accordance with the present invention;

FIGURE 13 depicts organic polymer (e.g., peptide) sequences obtained from PhD-C7C library selection against carbon planchet in accordance with the present invention;

FIGURE 14 depicts organic polymer (e.g., peptide) sequences obtained from PhD-12 library selection against carbon planchet in accordance with the present invention;

FIGURE 15 depicts organic polymer (e.g., peptide) sequences obtained from pHD-12 library selection against SWNT paste aggregates in accordance with the present invention;

FIGURE 16 depicts organic polymer (e.g., peptide) sequences obtained from PhD-12 library selection against HOPG in accordance with the present invention;

FIGURE 17 depicts binding efficiencies of various phage clones to SWNT paste aggregates in accordance with the present invention;

FIGURE 18 depicts binding efficiencies of various phage clones to carbon planchet in accordance with the present invention;

FIGURE 19 depicts confocal images of various phage clones bound to carbon planchet in accordance with the present invention;

FIGURE 20 depicts confocal images of various biotinylated peptides bound to carbon planchet in accordance with the present invention;

FIGURE 21 depicts confocal images of various phage clones bound to wet SWNT paste in accordance with the present invention;

FIGURE 22 depicts AFM images of phage clones on HOPG in accordance with the present invention;

FIGURE 23 depicts a schematic diagram of an SWNT purifying negative column;

FIGURE 24 depicts a schematic diagram of phage binding to SWNT (phage-SWNT);

FIGURE 25 depicts a schematic diagram of n-type SWNT modification using SWNT binding peptides;

FIGURE 26 depicts a schematic diagram for the application of SWNT as a drug releasing system; and

FIGURE 27 depicts a schematic diagram for the application of SWNTs in cancer medication.

DETAILED DESCRIPTION OF THE INVENTION

Although making and using various embodiments of the present invention are discussed in detail below, it should be appreciated that the present invention provides many applicable inventive concepts that can be embodied in a wide variety of specific contexts. The specific embodiments discussed herein are merely illustrative of specific ways to make and use the invention, and do not delimit the scope of the invention.

Terms used herein have meanings as commonly understood by a person of ordinary skill in the areas relevant to the present invention. Terms such as "a," "an," and "the" are not intended to refer to only a singular entity, but include the general class of which a specific example may be used for illustration. The terminology herein is used to describe specific embodiments of the invention, but their usage does not limit the invention, except as outlined in the claims.

The terminology herein is used to describe specific embodiments of the invention, but their usage does not limit the invention, except as outlined in the claims. As used throughout the present specification, the terms "quantum dots", "nanoparticles", and "particles" are used interchangeably.

As used herein, the term "biologic material" and/or "biologic material" refers to a virus, bacteriophage, bacteria, peptide, protein, amino acid, steroid, drug, chromophore, antibody, enzyme, single-stranded or double-stranded nucleic acid, and any chemical modifications thereof. The biologic material may self-assemble to form a dry thin film on the contacting surface of a substrate. Self-assembly may permit random or uniform alignment of the biologic material on the surface. In addition, the biologic

material may form a dry thin film that is externally controlled by solvent concentration, application of an electric and or magnetic field, optics, or other chemical or field interactions. As used herein, biologic material and "organic polymer" and "polymeric organic material" may be used interchangeably. As used herein, organic polymer refers to multiple units of organic material, wherein the organic material includes several "monomers" that may be the same or different. For example, proteins, antibodies, peptides, nucleic acids, chimeric molecules, drugs, and other carbon-containing materials known to exist in biologic systems (e.g., eukaryotic organisms) are illustrations of organic polymers. Other organic polymers may be derivatives or analogs of biologic polymers that contain one or more biologic monomers in combinations with synthetic monomers that may mimic those found naturally.

The term "inorganic molecule" or "inorganic compound" refers to compounds such as, e.g., indium tin oxide, doping agents, metals, minerals, radioisotope, salt, and combinations, thereof. Metals may include Ba, Sr, Ti, Bi, Ta, Zr, Fe, Ni, Mn, Pb, La, Li, Na, K, Rb, Cs, Fr, Be, Mg, Ca, Nb, Tl, Hg, Cu, Co, Rh, Sc, or Y. Inorganic compounds may include, e.g., high dielectric constant materials (insulators) such as barium strontium titanate, barium zirconate titanate, lead zirconate titanate, lead lanthanum titanate, strontium titanate, barium titanate, barium magnesium fluoride, bismuth titanate, strontium bismuth tantalite, and strontium bismuth tantalite niobate, or variations, thereof, known to those of ordinary skill in the art.

The term "organic molecule" or "organic compound" refers to compounds containing carbon alone or in combination, such

as nucleotides, polynucleotides, nucleosides, steroids, DNA, RNA, peptides, protein, antibodies, enzymes, carbohydrate, lipids, conducting polymers, drugs, and combinations, thereof. A drug may include an antibiotic, antimicrobial, anti-inflammatory, analgesic, antihistamine, and any agent used therapeutically or prophylactically against mammalian pathologic (or potentially pathologic) conditions.

The term "elemental carbon-containing molecule" generally refers to allotropic forms of carbon. Examples include, but are not limited to, diamond, graphite, activated carbon, $carbon_{60}$, carbon black, industrial carbon, charcoal, coke, and steel. Other examples include, but are not limited to carbon planchet, highly ordered pyrolytic graphite (HOPG), single-walled nanotube (SWNT), single-walled nanotube paste, multi-walled nanotube, multi-walled nanotube paste as well as metal impregnated carbon-containing materials.

As used herein, a "substrate" may be a microfabricated solid surface to which molecules attach through either covalent or non-covalent bonds and includes, e.g., silicon, Langmuir-Bodgett films, functionalized glass, germanium, ceramic, silicon, a semiconductor material, PTFE, carbon, polycarbonate, mica, mylar, plastic, quartz, polystyrene, gallium arsenide, gold, silver, metal, metal alloy, fabric, and combinations thereof capable of having functional groups such as amino, carboxyl, thiol or hydroxyl incorporated on its surface. Similarly, the substrate may be an organic material such as a protein, mammalian cell, antibody, organ, or tissue with a surface to which a biologic material may attach. The surface may be large or small and not necessarily uniform but should act as a contacting surface (not necessarily in monolayer). The substrate may be porous, planar or nonplanar. The substrate includes a contacting

surface that may be the substrate itself or a second layer (e.g., substrate or biologic material with a contacting surface) made of organic or inorganic molecules and to which organic or inorganic molecules may contact.

The inventors have previously shown that peptides may bind to semiconductor material. Semiconductor materials useful in binding peptides include, but are not limited to gallium arsenide, indium phosphate, gallium nitrate, zinc sulfide, aluminum arsenide, aluminum gallium arsenide, cadmium sulfide, cadmium selenide, zinc selenide, lead sulfide, boron nitride and silicon.

Semiconductor nanocrystals exhibit size and shape-dependent optical and electrical properties. These diverse properties result in their potential applications in a variety of devices such as light emitting diodes (LED), single electron transistors, photovoltaics, optical and magnetic memories, and diagnostic markers and sensors. Control of particle size, shape and phase is also critical in protective coatings such as car paint and in pigments such as house paints. The semiconductor materials may be engineered to be of certain shapes and sizes, wherein the optical and electrical properties of these semiconductor materials may best be exploited for use in numerous devices.

The present inventors have further developed a means of nucleating nanoparticles and directing their self-assembly. The main features of the peptides are their ability to recognize and bind technologically important materials with face specificity, to nucleate size-constrained crystalline semiconductor materials, and to control the crystallographic phase of nucleated nanoparticles. The peptides can also

control the aspect ratio of the materials and therefore, the optical properties.

Briefly, the facility with which biologic systems assemble immensely complicated structure on an exceedingly minute scale has motivated a great deal of interest in the desire to identify non-biologic systems that can behave in a similar fashion. Of particular value would be methods that could be applied to materials with interesting electronic or optical properties, but natural evolution has not selected for interactions between biomolecules and such materials.

The present invention is based on recognition that biologic systems efficiently and accurately assemble nanoscale building blocks into complex and functionally sophisticated structures with high perfection, controlled size and compositional uniformity.

One method of providing a random organic polymer pool is using a Phage-display library. A Phage-display library is a combinatorial library of random peptides containing between 7 and 12 amino acids fused to the pIII coat protein of M13 coliphage, providing different peptides that are reactive with crystalline semiconductor structures or other materials. Five copies of the pIII coat protein are located on one end of the phage particle, accounting for 10-16 nm of the particle. The phage-display approach provides a physical linkage between the peptide substrate interaction and the DNA that encodes that interaction.

Peptide sequences have been developed with affinities for various materials such as semiconductors, and elemental carbon-containing molecules such as carbon nanotubes and graphite. Five different single-crystal semiconductors, GaAs (100), GaAs (111)A, GaAs(111)B, InP(100) and Si(100), were

used in the following examples. These semiconductors allowed for systematic evaluation of the peptide interactions and confirmation of the general utility of the methodology of the present invention for different crystalline structures. In addition, elemental carbon-containing molecules such as carbon planchets, highly ordered pyrolytic graphite (HOPG), and single-walled nanotube (SWNT) paste were used.

Using a Phage-display library, protein sequences that successfully bound to the specific crystal were eluted from the surface, amplified by, e.g., a million-fold, and reacted against the substrate under more stringent conditions. This procedure was repeated between three and seven times to select the phage in the library with the most specific binding peptides. After, e.g., the third, fourth and fifth rounds of phage selection, crystal-specific phage were isolated and their DNA sequenced, identifying the peptide binding that is selective for the crystal composition (for example, binding to GaAs but not to Si) and crystalline face (for example, binding to (100) GaAs, but not to (111)B GaAs).

Twenty clones selected from GaAs(100) were analyzed to determine epitope binding domains by amino-acid functionality analysis to the GaAs surface. The partial peptide sequences of the modified pIII or pVIII protein are shown in FIGURE 1, revealing similar binding domains among peptides exposed to GaAs. With increasing number of exposures to a GaAs surface, the number of uncharged polar and Lewis-base functional groups increased. Phage clones from third, fourth and fifth round sequencing contained on average 30%, 40% and 44% polar functional groups, respectively, while the fraction of Lewis-base functional groups increased at the same time from 41% to 48% to 55%. The observed increase in Lewis bases, which should constitute only 34% of the functional groups in random

12-mer peptides from our library, suggests that interactions between Lewis bases on the peptides and Lewis-acid sites on the GaAs surface may mediate the selective binding exhibited by these peptides.

The expected structure of the modified 12-mers selected from the library may be an extended conformation, which seems likely for small peptides, making the peptide much longer than the unit cell (5.65 A°) of GaAs. Therefore, only small binding domains would be necessary for the peptide to recognize a GaAs crystal. These short peptide domains, highlighted in FIGURE 1, contain serine- and threonine-rich regions in addition to the presence of amine Lewis bases, such as asparagine and glutamine. To determine the exact binding sequence, the surfaces have been screened with shorter libraries, including 7-mer and disulphide constrained 7-mer libraries. Using these shorter libraries that reduce the size and flexibility of the binding domain, fewer peptide-surface interactions are allowed, yielding the expected increase in the strength of interactions between generations of selection.

Phage, tagged with streptavidin-labeled 20-nm colloidal gold particles bound to the phage through a biotinylated antibody to the M13 coat protein, were used for quantitative assessment of specific binding. X-ray photoelectron spectroscopy (XPS) elemental composition determination was performed, monitoring the phage substrate interaction through the intensity of the gold 4f-electron signal (FIGUREs 2a-c). Without the presence of the G1-3 phage, XPS confirmed that the antibody and the gold streptavidin did not bind to the GaAs(100) substrate. The gold-streptavidin binding was, therefore, specific to the peptide expressed on the phage and an indicator of the phage binding to the substrate. Using

XPS it was also found that the G1-3 sequence isolated from GaAs(100) bound specifically to GaAs(100) but not to Si(100)(see FIGURE 2a). In a complementary fashion the S1 clone, screened against the (100) Si surface, showed poor binding to the (100) GaAs surface.

Some GaAs sequences also bound the surface of InP (100), another zinc-blende structure. The basis of the selective binding, whether it is chemical, structural or electronic, is still under investigation. In addition, the presence of native oxide on the substrate surface may alter the selectivity of peptide binding.

The preferential binding of the G1-3 clone to GaAs(100), over the (111)A (gallium terminated) or (111)B (arsenic terminated) face of GaAs was demonstrated (Fig. 2b, c). The G1-3 clone surface concentration was greater on the (100) surface, which was used for its selection, than on the gallium-rich (111)A or arsenic-rich (111)B surfaces. These different surfaces are known to exhibit different chemical reactivities, and it is not surprising that there is selectivity demonstrated in the phage binding to the various crystal faces. Although the bulk termination of both 111 surfaces give the same geometric structure, the differences between having Ga or As atoms outermost in the surface bilayer become more apparent when comparing surface reconstructions. The composition of the oxides of the various GaAs surfaces is also expected to be different, and this in turn may affect the nature of the peptide binding.

The intensity of Ga 2p electrons against the binding energy from substrates that were exposed to the G1-3 phage clone is plotted in 2c. As expected from the results in Fig. 2b, the Ga 2p intensities observed on the GaAs (100), (111)A

and (111)B surfaces are inversely proportional to the gold concentrations. The decrease in Ga 2p intensity on surfaces with higher gold-streptavidin concentrations was due to the increase in surface coverage by the phage. XPS is a surface technique with a sampling depth of approximately 30 angstroms; therefore, as the thickness of the organic layer increases, the signal from the inorganic substrate decreases. This observation was used to confirm that the intensity of gold-streptavidin was indeed due to the presence of phage containing a crystal specific bonding sequence on the surface of GaAs. Binding studies were performed that correlate with the XPS data, where equal numbers of specific phage clones were exposed to various semiconductor substrates with equal surface areas. Wild-type clones (no random peptide insert) did not bind to GaAs (no plaques were detected). For the G1-3 clone, the eluted phage population was 12 times greater from GaAs(100) than from the GaAs(111)A surface.

The G1-3, G12-3 and G7-4 clones bound to GaAs(100) and InP(100) were imaged using atomic force microscopy (AFM). The InP crystal has a zinc-blende structure, isostructural with GaAs, although the In-P bond has greater ionic character than the GaAs bond. The 10-nm width and 900-nm length of the observed phage in AFM matches the dimensions of the M13 phage observed by transmission electron microscopy (TEM), and the gold spheres bound to M13 antibodies were observed bound to the phage (data not shown). The InP surface has a high concentration of phage. These data suggest that there are many factors involved in substrate recognition, including atom size, charge, polarity and crystal structure.

The G1-3 clone (negatively stained) is seen bound to a GaAs crystalline wafer in the TEM image (not shown). The data confirms that binding was directed by the modified pIII

protein of G1-3, not through non-specific interactions with the major coat protein. Therefore, peptides of the present invention may be used to direct specific peptide-semiconductor interactions in assembling nanostructures and heterostructures (Fig. 4).

X-ray fluorescence microscopy was used to demonstrate the preferential attachment of phage to a zinc-blende surface in close proximity to a surface of differing chemical and structural composition. A nested square pattern was etched into a GaAs wafer; this pattern contained 1-μm lines of GaAs, and 4-μm SiO_2 spacings in between each line (Figs. 3a, 3b). The G12-3 clones were interacted with the GaAs/SiO2 patterned substrate, washed to reduce non-specific binding, and tagged with an immuno-fluorescent probe, tetramethyl rhodamine (TMR). The tagged phage were found as the three red lines and the center dot, in Fig. 3b, corresponding to G12-3 binding only to GaAs. The SiO_2 regions of the pattern remain unbound by phage and are dark in color. This result was not observed on a control that was not exposed to phage, but was exposed to the primary antibody and TMR (Fig. 3a). The same result was obtained using non-phage bound G12-3 peptide.

The GaAs clone G12-3 was observed to be substrate-specific for GaAs over AlGaAs (Fig. 3c). AlAs and GaAs have essentially identical lattice constraints at room temperature, 5.66 A° and 5.65 A°, respectively, and thus ternary alloys of AlxGa1-xAs can be epitaxially grown on GaAs substrates. GaAs and AlGaAs have zinc-blende crystal structures, but the G12-3 clone exhibited selectivity in binding only to GaAs. A multilayer substrate was used, consisting of alternating layers of GaAs and of $Al_{0.98}Ga_{0.02}As$. The substrate material was cleaved and subsequently reacted with the G12-3 clone.

The G12-3 clones were labeled with 20-nm gold-streptavidin nanoparticles. Examination by scanning electron microscopy (SEM) shows the alternating layers of GaAs and $Al_{0.98}Ga_{0.02}As$ within the heterostructure (Fig. 3c). X-ray elemental analysis of gallium and aluminum was used to map the gold-streptavidin particles exclusively to the GaAs layers of the heterostructure, demonstrating the high degree of binding specificity for chemical composition. In Fig. 3d, a model is depicted for the discrimination of phage for semiconductor heterostructures, as seen in the fluorescence and SEM images (Figs 3a-c).

The present invention demonstrates the powerful use of phage-display libraries to identify, develop and amplify binding between organic peptide sequences and inorganic semiconductor substrates. This peptide recognition and specificity of inorganic crystals has been demonstrated above with GaAs, InP and Si, and has been extended to other substrates, including GaN, ZnS, CdS, Fe_3O_4, Fe_2O_3, CdSe, ZnSe and $CaCO_3$ using peptide libraries by the present inventors. Bivalent synthetic peptides with two-component recognition (Fig. 4) are currently being designed; such peptides have the potential to direct nanoparticles to specific locations on a semiconductor structure. These organic and inorganic pairs and potentially multivalent templates should provide powerful building blocks for the fabrication of a new generation of complex, sophisticated electronic structures.

EXAMPLE I. PEPTIDE CREATION, ISOLATION, SELECTION AND CHARACTERIZATION

Peptide selection. The phage display or peptide library was contacted with various materials such as a semiconductor crystal in Tris-buffered saline (TBS) containing 0.1% TWEEN-20, to reduce phage-phage interactions on the surface. After

rocking for 1 h at room temperature, the surfaces were washed with 10 exposures to Tris-buffered saline, pH 7.5, and increasing TWEEN-20 concentrations from 0.1% to 0.5%(v/v) as selection rounds progressed. The phage were eluted from the surface by the addition of glycine-HCl (pH 2.2) for 10 minutes to disrupt binding. The eluted phage solution was then transferred to a fresh tube and then neutralized with Tris-HCl (pH 9.1). The eluted phage were titred and binding efficiency was compared.

The phage eluted after third-round substrate exposure were mixed with their *Escherichia coli* ER2537 or ER2738 host and plated on LB XGal/IPTG plates. Since the library phage were derived from the vector M13mp19, which carries the lacZα gene, phage plaques were blue in color when plated on media containing Xgal (5-bromo-4-chloro-3-indoyl-β-D-galactoside) and IPTG (isopropyl-β-D-thiogalactoside). Blue/white screening was used to select phage plaques with the random peptide insert. Plaques were picked and DNA sequenced from these plates.

Substrate preparation. Substrate orientations were confirmed by X-ray diffraction, and native oxides were removed by appropriate chemical specific etching. The following etches were tested on GaAs and InP surfaces: NH_4OH: H_2O 1:10, HCl:H_2O 1:10, H_3PO_4: H_2O_2: H_2O 3:1:50 at 1 minute and 10 minute etch times. The best element ratio and least oxide formation (using XPS)for GaAs and InP etched surfaces was achieved using HCl: H_2O for 1 minute followed by a deionized water rinse for 1 minute. However, since an ammonium hydroxide etch was used for GaAs in the initial screening of the library, this etch was used for all other GaAs substrate examples. Si(100) wafers were etched in a solution of HF:H_2O 1:40 for one minute, followed by a deionized water rinse. All

surfaces were taken directly from the rinse solution and immediately introduced to the phage library. Surfaces of control substrates, not exposed to phage, were characterized and mapped for effectiveness of the etching process and morphology of surfaces by AFM and XPS.

Multilayer substrates of GaAs and of $Al_{0.98}Ga_{0.02}$ As were grown by molecular beam epitaxy onto (100) GaAs. The epitaxially grown layers were Si-doped (n-type) at a level of 5×10^{17} cm^{-3}.

Antibody and Gold Labeling. For the XPS, SEM and AFM examples, substrates were exposed to phage for 1 h in Tris-buffered saline then introduced to an anti-fd bacteriophage-biotin conjugate, an antibody to the pIII protein of fd phage, (1:500 in phosphate buffer, Sigma) for 30 minute and then rinsed in phosphate buffer. A streptavidin/20-nm colloidal gold label (1:200 in phosphate buffered saline (PBS), Sigma) was attached to the biotin-conjugated phage through a biotin-streptavidin interaction; the surfaces were exposed to the label for 30 minutes and then rinsed several times with PBS.

X-ray Photoelectron Spectroscopy (XPS). The following controls were prepared for the XPS examples to ensure that the gold signal seen in XPS was from gold bound to the phage and not non-specific antibody interaction with the GaAs surface. The prepared (100) GaAs surface was exposed to (1) antibody and the streptavidin-gold label, but without phage, (2) G1-3 phage and streptavidin-gold label, but without the antibody, and (3) streptavidin-gold label, without either G1-3 phage or antibody.

The XPS instrument used was a Physical Electronics Phi ESCA 5700 with an aluminum anode producing monochromatic

1,487-eV X-rays. All samples were introduced to the chamber immediately after gold-tagging the phage (as described above) to limit oxidation of the GaAs surfaces, and then pumped overnight at high vacuum to reduce sample outgassing in the XPS chamber.

Atomic Force Microscopy (AFM). The AFM used was a Digital Instruments Bioscope mounted on a Zeiss Axiovert 100s-2tv, operating in tip scanning mode with a G scanner. The images were taken in air using tapping mode. The AFM probes were etched silicon with 125-mm cantilevers and spring constants of 20±100 Nm -1 driven near their resonant frequency of 200±400 kHz. Scan rates were of the order of 1±5 mms -1. Images were leveled using a first-order plane to remove sample tilt.

Transmission Electron Microscopy (TEM). TEM images were taken using a Philips EM208 at 60 kV. The G1-3 phage (diluted 1:100 in TBS) were incubated with GaAs pieces (500 mm) for 30 minute, centrifuged to separate particles from unbound phage, rinsed with TBS, and resuspended in TBS. Samples were stained with 2% uranyl acetate.

Scanning Electron Microscopy (SEM). The G12-3 phage (diluted 1:100 in TBS) were incubated with a freshly cleaved hetero-structure surface for 30 minute and rinsed with TBS. The G12-3 phage were tagged with 20-nm colloidal gold. SEM and elemental mapping images were collected using the Norian detection system mounted on a Hitachi 4700 field emission scanning electron microscope at 5 kV.

EXAMPLE II. SELECTION OF PARTICLE AND ORIENTATION SPECIFIC PEPTIDES

It has been found that semiconductor nanocrystals exhibit size and shape-dependent optical and electrical

properties may result in their potential applications in a variety of devices such as light emitting diode (LED), single electron transistor, photovoltaics, optical and magnetic memory, diagnostic markers and sensors. Control of particle size shape and phase is also critical in protective coatings, and pigments (car paints, house paints). To exploit these optical and electrical properties, it is necessary to synthesize crystallized semiconductor nanocrystals with, among other things, tailored size and shape.

The present invention includes compositions and methods for the selection and use of peptides that can: (1) recognize and bind technologically important materials with face specificity; (2) nucleate size constrained crystalline semiconductor materials; (3) control the crystallographic phase of nucleated nanoparticles; and (4) control the aspect ratio of the nanocrystals and, e.g, their optical properties.

Examples of materials used in this example were the Group II-VI semiconductors, which include materials such as: zinc sulfide, cadmium sulfide, cadmium selenium and zinc selenium. Size and crystal control could also be used with cobalt, manganese, iron oxides, iron sulfide, and lead sulfide as well as other optical and magnetic materials. Using the present invention, the skilled artisan can create inorganic-biologic material building blocks that serve as the basis for a radically new method of fabrication of complex electronic devices, optoelectronic device such as light emitting displays, optical detectors and lasers, fast interconnects, wavelength-selective switches, nanometer-scale computer components, mammalian implants and environmental and in situ diagnostics.

FIGUREs 4-8 depict the expression of peptides using, e.g., a phage display library to express the peptides that will bind to the semiconductor material. Those of skill in the art of molecular biology will recognize that other expression systems may be used to "display" short or even long peptide sequences in a stable manner on the surface of a protein. Phage display may be used herein as an example. The phage-display library is a combinatorial library of random peptides containing between 7 and 12 amino acids. The peptides may be fused to, or form a chimera with, e.g., the pIII coat protein of M13 coliphage. The phage provided different peptides that were reacted with crystalline semiconductor structures. M13 pIII coat protein is useful because five copies of the pIII coat protein are located on one end of the phage particle, accounting for 10-16 nm of the particle. The phage-display approach provided a physical linkage between the peptide substrate interaction and the DNA that encodes that interaction. The semiconductor materials tested included ZnS, CdS, CdSe, and ZnSe.

To obtain peptides with specific binding properties, protein sequences that successfully bound to the specific crystal were eluted from the surface, amplified by, e.g., a million-fold, and reacted against the substrate under more stringent conditions. This procedure was repeated five times to select the phage in the library with the most specific binding. After, e.g., the third, fourth and fifth rounds of phage selection, crystal-specific phage were isolated and the DNA sequenced to decipher the peptide motif responsible for surface binding.

In one example of the present invention, two different peptides were found to nucleate two different phases of quantum dots. A linear 12-mer peptide, Z8, has been found

that grows 3-4 nm particles of the cubic phase of zinc sulfide. A 7-mer disulfide constrained peptide, A7, has been isolated that grows nanoparticles of the hexagonal phase of ZnS. In addition, these peptides affect the aspect ratio (shape) of the nanoparticles grown. The A7 peptide has this "activity" while is it still attached to p3 of the phage or attached as a monolayer on gold. In addition phage/semiconductor nanoparticle nanowires wires were grown using an A7 fusion to the p8 protein on the virus coat. The nanoparticles grown on the phage coat show perfect crystallographic alignment of ZnS particles.

Peptides controlling nanoparticle size, morphology and aspect ratio. Phage that display a shape-controlling amino acid sequence were isolated, characterized and selected that specifically bind to ZnS, CdS, ZnSe and CdSe crystals. The binding affinity and discrimination of these peptides was tested and based on the results, peptides will be engineered for higher affinity binding. To conduct the tests, the phage library was screened against mm-size polycrystalline ZnS pieces. Binding clones were sequenced and amplified after third, fourth and fifth round selections. Sequences were analyzed and clones were tested for the ability of peptides that bind ZnS to nucleate nanoparticles of ZnS.

The clones designated Z8, A7 and Z10 clone were added to ZnS synthesis experiments to attempt to control ZnS particle size and monodispersity at room temperature in aqueous conditions. The ZnS-specific clones were interacted with Zn^{+2} ions in millimolar concentrations of $ZnCl_2$ solution. The ZnS-specific peptide bound to the phage acts as a capping ligand, controlling crystalline particle size as ZnS is formed upon addition of Na_2S to the phage-$ZnCl_2$ solution.

Upon introduction of millimolar concentrations of Na_2S, crystalline material was observed to be in suspension. The suspensions were analyzed for particle size and crystal structures using transmission electron microscopy (TEM) and electron diffraction (ED). The TEM and ED data revealed that the addition of the ZnS-specific peptide bound to the phage clone affected the particle size of the forming ZnS crystals.

Crystals grown in the presence of the ZnS were observed to be approximately 5 nm in size and discrete particles. Crystals grown without the ZnS phage clones were much larger (>100 nm) and exhibited a range of sizes.

TABLE 1. Binding domains of ZnS specific clones (written amino to carboxy terminus).

A7	Asn Asn Pro Met His Gln Asn Cys (SEQ ID NO.:232)
Z8	Val Ile Ser Asn His Ala Glu Ser Ser Arg Arg Leu (SEQ ID NO.:72)
Z10	Ser Gly Pro Ala His Gly Met Phe Ala Arg Pro Leu (SEQ ID NO.:233)

TABLE 2. Binding domains of CdS specific clones (written amino to carboxy terminus).

E1:	Cys His Ala Ser Asn Arg Leu Ser Cys (SEQ ID NO.:12)
E14:	Gly Thr Phe Thr Pro Arg Pro Thr Pro Ile Tyr Pro (SEQ ID NO.:14)
E15:	Gln Met Ser Glu Asn Leu Thr Ser Gln Ile Glu Ser (SEQ ID NO.:15)
JCW-96:	Ser Pro Gly Asp Ser Leu Lys Lys Leu Ala Ala Ser (SEQ ID NO.:28)

JCW-106: Ser Leu Thr Pro Leu Thr Thr Ser His Leu Arg Ser (SEQ ID NO.:30)

JCW-137: Ser Leu Thr Pro Leu Thr Thr Ser His Leu Arg Ser (SEQ ID NO.:30)

JCW-182: Cys Thr Tyr Ser Arg Leu His Leu Cys (SEQ ID NO.:234)

JCW-201: Cys Arg Pro Tyr Asn Ile His Gln Cys (SEQ ID NO.:235)

JCW-205: Cys Pro Phe Lys Thr Ala Phe Pro Cys (SEQ ID NO.:236)

The peptide insert structure expressed during phage generation, e.g., a 12-mer linear and 7-mer constrained libraries with a disulfide bond have been used, with similar results.

Peptides selected for ZnS using a 12 amino acid linear library verses a 7 amino acid constrained loop library had a significant effect on both the crystal structure of ZnS and the aspect ratio of the ZnS nanocrystals.

High resolution lattice images of nanoparticles grown in the presence of phage displaying 12 mer linear peptides that had been selected for ZnS revealed the crystals grew 3-4 nm spheres (1:1 aspect ratio) of the cubic (zinc-blende) form of ZnS. In contrast, the 7 mer constrained peptides selected to bind ZnS grew elliptical particles and wires (2:1 aspect ratio and 8:1 aspect ratio) of the hexagonal (wurzite) form of ZnS. Thus, the nanocrystal properties could be engineered by adjusting the length and sequence of the peptide. Further, electron diffraction patterns of the crystals revealed that peptides from different clones can stabilize the two different crystal structures of ZnS. The Z8 12 mer

peptide stabilized the zinc-blende structure and the A7 7 mer constrained peptide stabilized the wurzite structure.

FIGURE 10 shows the sequence evolution for ZnS peptides after the third, fourth and fifth rounds of selection. For peptide selection with the 7 mer constrained library, the best binding peptide sequence was obtained by the fifth round of selection. This sequence was named A7. Approximately thirty percent of the clones isolated after the fifth round of selection had the A7 sequence. The ASN/GLN at position number 7 was found to be significant starting from the third round of selection. In the fourth round of selection, the ASN/GLN also became important in position numbers 1 and 2. This importance increased in round 5. Throughout rounds 3, 4, and 5, a positive charge became prominent at position 2. FIGURE 11 depicts the amino acid substitutions after the fifth round of selection in accordance with the present invention.

Site-directed mutagenesis is being conducted in the A7 sequence to test for a change in binding affinity. Mutations being tested include: position 3: his ala; position 4: met ala; position 2: gln ala; and position 6: asn ala. These changes may be made to the peptide concurrently, individually or in combinations.

The amino acid sequence motif defined for ZnS binding is, therefore (written amino to carboxy terminus): amide-amide-Xaa-Xaa-positive-amide-amide or ASN/GLN - ASN/GLN - PRO - MET - HIS - ASN/GLN - ASN/GLN (SEQ ID NO.:237).

The clones isolated for ZnS through binding studies showed preferential interaction to ZnS, the substrate against which they had been raised, versus foreign clones and foreign substrates.

Interactions of different clones with different substrates such as FeS, Si, CdS and ZnS showed that the clones isolated through binding studies for ZnS showed preferential interaction to the ZnS against which they had been raised. Briefly, after washings and infection, phage titers were counted and compared. For Z8 and Z10, no titer count was evident on any substrate except ZnS. Wild-type clones with no peptide insert were used as a control to verify that the engineered insert had indeed mediated the interaction of interest. Without the peptide, no specific binding occurred, as was evidenced by a titer count of zero.

Using the same binding method that was used for, several different ZnS clones were compared to each other. Clones having different peptide inserts at the same concentration were interacted with a similar sized piece of ZnS for one hour. The substrate-phage complex was washed repeatedly, and the bound phage was eluted by changing the pH. The eluate was infected into bacteria and the plaques were counted after an overnight incubation. Z8 showed the greatest affinity for the ZnS of the 12 mer linear peptides selected. The wild-type did not show binding to the ZnS crystal. The Z8, Z10 and the wild-type peptides did not bind to the Si, FeS or CdS crystals.

The synthesis and assembly of nanocrystals on peptide functionalized surfaces was determined. The A7 peptide was tested alone for the ability to control the structure of ZnS. The A7 peptide, which specifically selected and grew ZnS crystals when attached to the phage, was applied in the form of a functionalized surface on a gold substrate that could direct the formation of ZnS nanocrystals from solution. A process that is used to prepare self-assembled monolayer was employed to prepare a functionalized surface.

To determine the ability and selectivity of A7 in the formation of ZnS nanocrystals, different kinds of surfaces with different surface chemistry on the gold substrate were interfaced with ZnS precursor solution. $ZnCl_2$ and Na_2S were used as the ZnS precursor solutions. CdS precursor solution of $CdCl_2$ and Na_2S was used as the CdS source. The crystals that formed on the four surfaces were characterized by SEM/EDS and TEM observation.

Control surface 1 consisted of a blank gold substrate. After being aged for 70 h in either ZnS solution or CdS solution, crystals formation was not observed. Control surface 2 consisted of a 2-mercaptoethyamine self-assembled monolayer on a gold substrate. This surface could not induce the formation of ZnS and CdS nanocrystals. In a few places, ZnS precipitates were observed. For the CdS system, sparsely distributed 2 micron CdS crystals were observed. Precipitation of these crystals occurred when the concentrations of both Cd^{+2} and S^{-2} were at 1×10^{-3} M.

The third surface tested was an A7-only functionalized gold surface. This surface was able to direct the formation of 5 nm ZnS nanocrystals, but could not direct the formation of CdS nanocrystals.

The fourth surface tested was an A7-amine functionalized gold surface that was prepared by aging control surface 2 in A7 peptide solution. The ZnS crystals formed on this surface were 5 nm and the CdS crystals were 1-3 μm. The CdS crystals could also be formed on the amine-only surface.

From the results of the four surfaces, the A7 peptide could direct the formation of ZnS nanocrystals for which it was selected, but could not direct the formation of CdS

nanocrystals. Further, peptides selected against CdS could nucleate nanoparticles of CdS.

The peptides that could specifically nucleate semiconductor materials were expressed on the p8 major coat protein of M13. The p8 proteins are known to self-assemble into a highly oriented, crystalline protein coat. The hypothesis was that if the peptide insert could be expressed in high copy number, the crystalline structure of the p8 protein would be transferred to the peptide insert. It was also predicted that if the desired peptide insert maintained a crystal orientation relative to the p8 coat, then the crystals that nucleated from this peptide insert should grow nanocrystals that are crystallographically related. This prediction was tested and confirmed using high resolution TEM.

FIGURE 12 shows a schematic diagram of the p8 and p3 inserts used to form nanowires. ZnS nanowires were made by nucleating ZnS nanoparticles off of the A7 peptide fusion along the p8 protein coat of M13 phage. The ZnS nanoparticles coated the surface of the phage. The HR TEM image of ZnS nucleated on the coats of M13 phage that have the A7 peptide insert within the p8 protein showed that the nanocrystals nucleated on the coat of the phage were perfectly oriented. It is not clear whether the phage coat was a mixture of the p8-A7 fusion coat protein and the wild-type p8 protein. Similar experiments were performed with the Z8 peptide insert, and although the ZnS crystals were also nucleated along the phage, they were not orientated relative to each other.

Atomic force microscopy (AFM) was used to imagine the results, which indicated that the p8-A7 self-assembling

crystals coated the surface of the phage, creating nanowires along the crest of the chimeric protein at the location of the A7 peptide sequence (data not shown). Nanowires were made by nucleating ZnS nanoparticles at the sites of the p8-A7 fusion along the coat of M13.

Nanocrystal nucleation of ZnS on the coat M13 phage that have the A7 peptide insert in the p8 protein was confirmed by high resolution TEM. Crystal nucleation was achieved despite the fact that some wild type p8 protein was found mixtured in with the p8-A7 fusion coat protein. The nanocrystals nucleated on the coat of the phage were perfectly orientated, as evidenced by lattice imaging (data not shown). The data demonstrates that peptides can be displayed in the major coat protein with perfect orientation conservation, and that these orientated peptides can nucleate orientated mondispersed ZnS semiconductor nanoparticles.

The cumulative data showed that some peptides could be displayed in the major coat protein with perfect orientation conservation and that these peptides could nucleate orientated ZnS semiconductor nanoparticles.

Peptide selection. The phage display or peptide library was contacted with the semiconductor, or other crystals, in Tris-buffered saline (TBS) containing 0.1% TWEEN-20, to reduce phage-phage interactions on the surface. After rocking for 1 hour at room temperature, the surfaces were washed with 10 exposures to Tris-buffered saline, pH 7.5, and increasing TWEEN-20 concentrations from 0.1% to 0.5%(v/v) as selection rounds progressed. The phage display was eluted from the surface by the addition of glycine-HCl (pH 2.2) for 10 minutes to disrupt binding. The eluted phage solution was then transferred to a fresh tube and then neutralized with

Tris-HCl (pH 9.1). The eluted phage were titred and binding efficiency was compared.

The phage eluted after the third-round of substrate exposure were mixed with an *Escherichia coli* ER2537 or ER2738 host and plated on Luria-Bertani (LB) XGal/IPTG plates. Since the library phage were derived from the vector M13mp19, which carries the lacZα gene, phage plaques, or infection events, were blue in color when plated on media containing Xgal (5-bromo-4-chloro-3-indoyl-β-D-galactoside) and IPTG (isopropyl-β-D-thiogalactoside). Blue/white screening was used to select phage plaques with the random peptide insert. DNA from these plaques was isolated and sequenced.

Atomic Force Microscopy (AFM). The AFM used was a Digital Instruments Bioscope mounted on a Zeiss Axiovert 100s-2tv, operating in tapping mode. The images were taken in air using tapping mode. The AFM probes were etched silicon with 125-mm cantilevers and spring constants of 20±100 Nm^{-1} driven near their resonant frequency of 200±400 kHz. Scan rates were of the order of 1±5 mms^{-1}. Images were leveled using a first-order plane to remove sample tilt.

Transmission Electron Microscopy (TEM). TEM images were taken on JEOL 2010 and JEOL200CX transmission electron microscopes. The TEM grids used were carbon on gold. No stain was used. After the samples were grown, the reaction mixture was concentrated on molecular weight cut-off filters and washed four times with sterile water to wash away any excess ions or non-phage bond particles. After concentrating to 20-50 µl, the sample was then dried down on TEM or AFM specimen grids.

EXAMPLE III. BIOLOGIC MATERIALS WITH AFFINITIES FOR ELEMENTAL CARBON-CONTAINING MOLECULES

In this example, seven- and twelve-mer peptide sequences with affinities to carbon planchets, highly ordered pyrolytic graphite (HOPG), and single-walled nanotube (SWNT) paste were determined using phage display. Among the phage clones selected from biopanning, clones Graph5-01 (N'-WWSWHPW-C') (SEQ ID NO:238) and Graph53-01 (N'-HWSWWHP-C') (SEQ ID NO:239) bound with greatest efficiencies to carbon planchets in phage binding studies. Clone Hipco12R44-01 (N'-DMPRTTMSPPPR-C') (SEQ ID NO:196) bound best to SWNT paste.

The relative abilities of these phage to bind to their corresponding substrates was verified by labeling the phage with fluorescein-labeled anti-M13 phage antibodies and visualizing them on their substrates using confocal microscopy. Confocal microscopy was also used to visualize the binding of the substrates to fluorescently-labeled synthetic peptides containing these substrate-specific sequences. Clone Graph5-01 displayed some crossreactivity to HOPG, as determined by AFM. Examples of additional methodology is described below.

Biopanning. Carbon planchetts (obtained from Ted Pella, Inc., with dimensions at about 12.7 mm diam x 1.6 mm thick; in pieces at about 5 x 2 x 1.6 mm) and highly ordered pyrolytic graphite (HOPG) (obtained from the University of Texas at Austin) were used as graphite sources for biopanning. SWNT paste was molded into cigar-shaped aggregates (at least about 0.1 g wet) and dessicated for at least about one night before use in biopanning (final dried mass was at about 0.05 g). PhD-C7C and PhD-12mer libraries were obtained from New England Biolabs, Inc. (Beverly, MA), and biopanning was performed according to manufacturer instructions. Biopanning for each substrate was repeated at least once.

Phage Clone Nomenclature. The names of phage clones selected against carbon planchets were prefaced by "Graph." Phage clones selected against SWNT paste were prefaced by "Hipco." Phage clones selected against HOPG were prefaced by "HOPG." Selected clones with 12-mer inserts were named, (Substrate)12R(round#)(round repeat#)-(SEQ ID NO:); whereas clones with constrained 7-mer inserts were named, (Substrate)(round#)(round repeat#)-(SEQ ID NO:).

Peptides. The biotinylated peptide Hipco2B (N'-DMPRTTMSPPPRGGGK-C'-biotin) (SEQ ID NO.:244) was synthesized by Genemed Synthesis, Inc. (San Francisco, CA). Biotinylated peptides Graphite1B (N'-ACWWSWHPWCGGGK-C'-biotin) (SEQ ID NO:240), JH127B (N'-ACDSPHRHSCGGGK-C'-biotin)(SEQ ID NO:241), and JH127MixB (N'-ACPRSSHDHCGGGK-C'-biotin) (SEQ ID NO:242) were synthesized by the ICMB Protein Microanalysis Facility (University of Texas at Austin) and purified by reversed phase HPLC (HiPore RP318 250x10mm column, BioRad, Hercules, CA, acetonitrile gradient). Disulfide bond formation between the cysteines of the Graphite1B peptide was performed by iodine oxidation according to methods known in the art of chemistry, resulting in the cyclized Graphite1B peptide. The purity and molecular masses of the peptides were verified using electrospray ionization mass spectrometry (Esquire-LC00113, Bruker Daltonics, Inc., Billerica, MA).

Phage Binding Studies. Dessicated, flat, square-shaped aggregates of SWNT paste (at least about 0.05g wet and 0.0025g dried) and at least about 0.04 g carbon planchet pieces were used for binding studies. Phage clones were amplified and titered (according to phage library manufacturer instructions) at least twice before use. Equal amounts (at least about $5x10^{10}$ pfu) of each phage clone were separately incubated with the SWNT/carbon planchet (e.g., as

aggregates) in 1 ml TBS-T [50 mM Tris, 150 mM NaCl, pH 7.5, 0.1% Tween-20] for 1 hour at room temperature with rocking in a microcentrifuge tube. The aggregate surfaces were then washed 9-10 times with TBS-T (1 ml per wash), and phage were eluted off the surfaces by exposure to 0.5 ml 0.2 M Glycine HCl (pH 2.2) for 8 minutes. The eluted phage were immediately transferred to a fresh tube, neutralized with 0.15 ml 1 M Tris HCl (pH 9.1), and then titered in duplicate. Each binding experiment was performed twice. In one embodiment of the present invention, repeated binding studies using SWNT aggregates using the same aggregates (ones used for the original experiments) included an initial wash with 1 ml 100% ethanol for 1 hour and then twice with 1 ml water).

Confocal Microscopy. Phage clones were amplified and titered (according to phage library manufacturer instructions) at least twice before use. Equal amounts (5 x 10^9 pfu) of each phage clone were separately incubated with pieces of carbon planchet or small amounts of wet SWNT paste in 0.2-0.3 ml TBS-T for 1 hour in a microcentrifuge tube with occasional shaking. The carbon planchet/SWNT aggregate(s) were then washed twice with TBS-T (1 ml per wash), incubated for 45 minutes with 0.2-0.3 ml of biotinylated mouse monoclonal anti-M13 antibody (1:100 dilution in TBS-T, Exalpha Biologicals, Inc., Boston, MA). The aggregates were then washed twice with TBS-T (1 ml per wash), incubated for 10 minutes with 0.2-0.3ml streptavidin-fluorescein (1:100 dilution in TBS-T from Amersham Pharmacia Biotech, Uppsala, Sweden), and then washed twice with TBS-T (1 ml per wash). Excess fluid was then removed from the aggregates. The SWNT paste was resuspended in Gel/Mount (Biomedia Corp., Foster City, CA) and mounted on a glass slide with a No. 1 coverslip. The carbon planchets were mounted on a glass slide with vacuum grease, covered with Gel/Mount, and topped

with a coverslip. For the SWNT paste samples, centrifugation was required for each labeling and washing step.

Peptides (at least about 1 mg/ml) were separately incubated with pieces of carbon planchet or small amounts of wet SWNT paste in 0.15 ml TBS-T for 1 hour in a microcentrifuge tube with occasional shaking. Original 10 mg/ml stocks of Hipco2B were found to be soluble in 55% acetonitrile and cyclized and noncyclized Graphite1B in 45% acetonitrile. Upon dilution in TBS-T, these peptides formed white precipitates. The substrates were then washed 2-3 times with TBS-T (1 ml per wash), incubated for 15 minutes with 0.15 ml streptavidin-fluorescein (1:100 dilution in TBS), and then washed 2-3 times with TBS (1 ml per wash). Excess fluid was removed from the substrates. The SWNT paste was resuspended in Gel/Mount and mounted on a glass slide with a coverslip. The carbon planchets were mounted on a glass slide with vacuum grease, covered with Gel/Mount, and topped with a coverslip. For the SWNT paste samples, centrifugation was required for each labeling and washing step.

Confocal images were obtained on a Leica TCS 4D Confocal Microscope (ICMB Core Facility, University of Texas at Austin). Images were presented as maximum intensity composites.

AFM. Phage clones were amplified and titered (according to phage library manufacturer instructions) at least twice before use. Equal amounts ($5x10^9$ pfu) of each phage clone were separately incubated with freshly cleaved layers of HOPG in 2 ml TBS for 1 hour with rocking in 35mm x 10mm petri dishes. The substrates were then transferred to microcentrifuge tubes, washed twice with water (1 ml per

wash), and dessicated overnight. Images were taken in air using tapping mode on a Multimode Atomic Force Microscope (Digital Instruments, Santa Barbara, CA).

Biopanning Sequences. M13 phage libraries with 12-mer and constrained 7-mer sequences inserted into their pIII coat protein were used to select clones with specificities toward carbon planchets, HOPG, and SWNT paste.

For Carbon Planchet. Selection using the PhD-C7C library against carbon planchets yielded a dominant phage clone with the peptide insert sequence N'-WWSWHPW-C' (SEQ ID NO:238) by the 4th round as shown in FIGURE 13. Upon repeating the selection, a similar dominant sequence N'-HWSWWHP-C' (SEQ ID NO:239) and a less dominant sequence N'-YFSWWHP-C' (SEQ ID NO:243) were obtained by the 4th round. Selection with the PhD-12 library yielded the consensus sequence N'-NHRIWESFWPSA-C' (SEQ ID NO:172) by the 5th round, and repeating the selection yielded the sequences N'-VSRHQSWHPHDL-C' (SEQ ID NO:179) and N'-YWPSKHWWWLAP-C' (SEQ ID NO:180) by the 6th round, as indicated in FIGURE 14. These sequences were rich in aromatic residues and commonly included the residues S, W, H, and P. One one embodiment of the present invention, N'-SHPWNAQRELSV-C' (SEQ ID NO:178) was observed in round 5 of selection with the PhD-12 library, but was a contaminating sequence from biopanning against SWNT paste; the sequence disappeared in subsequent rounds.)

For SWNT Paste. Biopanning with the PhD-C7C library against SWNT paste was unsuccessful due to the domination of the selected phage by the "wildtype" phage clone (containing no peptide insert in pIII). As shown in FIGURE 15, the consensus sequence N'-SHPWNAQRELSV-C' (SEQ ID NO:178) was obtained by selection using the PhD-12 library by the 4th

round, and second and third repeats of the selection process yielded the sequences N'-LLADTTHHRPWT-C' (SEQ ID NO:192), N'-DMPRTTMSPPPR-C' (SEQ ID NO:196), and N'-TKNMLSLPVGPG-C' (SEQ ID NO:195).

For HOPG. Selection against HOPG using the PhD-C7C library was not performed, but the PhD-12 library yielded the dominant sequence N'-TSNPHTRHYYPI-C' (SEQ ID NO:219) and the less dominant sequences N'-KMDRHDPSPALL-C' (SEQ ID NO:221) and N'-SNFTTQMTFYTG-C' (SEQ ID NO:220) by the 5th round as shown in FIGURE 16. (NOTE: The sequence N'- LLADTTHHRPWT-C' (SEQ ID NO:192) was also observed in the first selection but was found to be a contaminating sequence from biopanning against SWNT paste.)

An example of many major sequences obtained from biopanning is presented in TABLE 3.

TABLE 3: Example of consensus sequences (N'-to C'-terminus) obtained from biopanning

Library	Carbon Planchet	SWNT Paste	HOPG
PhD-C7C	WWSWHPW (SEQ ID NO:238)	Unsuccessful	Not performed
	HWSWWHP (SEQ ID NO:239)		
	YFSWWHP (SEQ ID NO:243)		
PhD-12	NHRIWESFWPSA (SEQ ID NO:245)	SHPWNAQRELSV (SEQ ID NO:178)	TSNPHTRHYYPI (SEQ ID NO:219)
	VSRHQSWHPHDL (SEQ ID NO:179)	LLADTTHHRPWT (SEQ ID NO:192)	KMDRHDPSPALL (SEQ ID NO:221)
	YWPSKHWWWLAP (SEQ ID NO:180)	DMPRTTMSPPPR (SEQ ID NO:196)	SNFTTQMTFYTG (SEQ ID NO:220)
		TKNMLSLPVGPG (SEQ ID NO:195)	

Phage binding studies. The relative binding efficiencies of the different phage clones determined from biopanning were tested by exposing carbon planchet pieces and SWNT paste aggregates separately to equal numbers ($5x10^{10}$ pfu)

of each phage clone for 1 hour and titering the amount of each clone left bound to the substrate surfaces after washing with TBS-T. Bound phage were then eluted from the substrates with 0.2 M Glycine HCl, pH 2.2 and quantified by titering. The clones used for these experiments are listed in TABLE 4. The A7 (constrained 7-mer insert) and Z8 (12-mer insert) clones and "wildtype" clone were used as negative controls.

TABLE 4. PIII inserts of phage clones used for phage binding studies

Phage Clone	Library Source	pIII insert (N'- to C'-terminus)
Hipco12R4-01	PhD-12	SHPWNAQRELSV (SEQ ID NO:178)
Hipco12R42-01	PhD-12	LLADTTHHRPWT (SEQ ID NO:192)
Hipco12R44-01	PhD-12	DMPRTTMSPPPR (SEQ ID NO:196)
Hipco12R44-03	PhD-12	TKNMLSLPVGPG (SEQ ID NO:195)
Graph5-01	PhD-C7C	WWSWHPW (SEQ ID NO:238)
Graph53-01	PhD-C7C	HWSWWHP (SEQ ID NO:239)
Graph53-05	PhD-C7C	YFSWWHP (SEQ ID NO:243)
Graph12R5-01	PhD-12	NHRIWESFWPSA (SEQ ID NO:245)
Graph12R62-01	PhD-12	VSRHQSWHPHDL (SEQ ID NO:179)
Graph12R62-02	PhD-12	YWPSKHWWWLAP (SEQ ID NO:180)
A7	PhD-C7C	NNPHMQN (SEQ ID NO:229)
Z8	PhD-12	VISNHAESSRRL (SEQ ID NO:230)
Graph4-18	PhD-12, -C7C	no insert ("wildtype")

As shown in FIGURE 17 (panels A and B), phage clone Hipco12R44-01 bound to SWNT paste in higher numbers than all other SWNT- or carbon planchet-specific clones, whereas clones Graph5-01 and Graph53-01, as shown in FIGURE 18, bound with greatest efficiencies to carbon planchet. Little crossreactivity to SWNT paste was observed by the clones selected against carbon planchet. In addition, clones selected against SWNT paste were not crossreactive with carbon planchet.

While several consensus sequences were obtained from the biopanning process, not all of the phage clones selected by biopanning may be efficient binders (*i.e.*, "efficient" meaning having affinities to the substrates greater than that of the wildtype clone, as determined by this type of binding or affinity study). The inability to completely remove all binding phage from the substrates using the elution buffer (0.2 M Glycine HCl, pH 2.2) in these binding studies may be a possible source of error in the interpretation of these experiments. These results may also illustrate the significance of selecting and testing several consensus sequences for each substrate (*i.e.*, repeated biopanning may yield better sequences).

Visualization of Phage and Peptides on Substrates by Confocal Microscopy

Carbon Planchet. As shown in FIGURE 19, the binding of the carbon planchet-specific phage clones (Graph5-01 phage and Graph53-01 phage) to their substrates was visualized by exposing carbon planchet pieces separately to equal numbers ($5x10^9$ pfu) of each clone for 1 hour, labeling the phage with a biotinylated anti-M13 antibody, labeling the antibody with streptavidin-fluorescein, and visualizing the complexes by confocal microscopy. (All images 250μmx250μm unless noted.) Phage clones Hipco12R44-01, JH127 (97μmx97μm) (from Sandra Whaley, with constrained pIII insert N'-DSPHRHS-C') (SEQ ID NO:231), and wildtype (Graph4-18, no insert) clone were used as negative controls. Consistent with the results of the above phage binding studies, carbon planchet bound most efficiently to clone Graph5-01 and, to a lesser extent, to Graph53-01 as shown in FIGURE 19. A considerable amount of crossreactivity was observed between the substrate and clone

JH127, but very little binding was observed between carbon planchet and clone Hipco12R44-01 or the wildtype clone.

The binding of carbon planchet to peptides with sequences corresponding to the pIII inserts of the phage clones above was also visualized by confocal microscopy. Equal amounts (1 mg/ml) of cyclized peptide Graphite1B (corresponding to clone Graph5-01), noncyclized peptide Graphite1B, peptide Hipco2B (corresponding to clone Hipco12R44-01), peptide JH127B (corresponding to clone JH127), and peptide JH127MixB (also corresponding to clone JH127 but having a mixed amino acid sequence) were separately exposed to carbon planchet pieces for 1 hour and then labeled with streptavidin-fluorescein.

As shown in FIGURE 20, a detectable amount of background fluorescence was observed in the sample incubated with no peptide, indicating that nonspecific binding occurred between the streptavidin-fluorescein and substrate. This result is most likely due to insufficient washing in this particular experiment, since a similar sample that was not exposed to phage nor peptide in the experiment depicted in FIGURE 19 exhibited no background fluorescence. Despite this background fluorescence, the sample exposed to noncyclized Graphite1B exhibited a higher degree of fluorescence than the other samples. In contrast, the fluorescence displayed by the cyclized Graphite1B and Hipco2B samples was no higher than the background, indicating that the cyclization of Graphite1B interfered with substrate binding (images 250μmx250μm). A slightly higher degree of binding was observed between the substrate and peptides JH127B and JH127MixB. The amino acid residues common to the Graphite1B, JH127B, and JH127MixB peptides are S, P, and H. Future confocal experiments visualizing peptide binding to carbon

planchet should utilize higher concentrations of peptide to enhance fluorescence and better washing procedures to decrease background.

SWNT Paste. The binding of SWNT paste to the phage clone with the highest affinity to SWNT paste (Hipco12R44-01) was also visualized by confocal microscopy as shown in FIGURE 21 (images 250μmx250μm). The Graph5-01 and wildtype (Graph4-18, no insert) clones were used as negative controls. The Hipco12R44-01 clone showed a high degree of fluorescence, but considerable fluorescence was also observed in the control samples. No background fluorescence was observed in the absence of phage, indicating that the fluorescence in the Graph5-01 and wildtype samples was not due to nonspecific substrate binding by the antibody or streptavidin-fluorescein. Although these confocal binding studies utilized concentrations of phage ($5x10^9$ pfu in 0.2-0.3 ml = 1.7-2.5 x 10^{10} pfu/ml) that were on the same order of magnitude as those used in the phage binding studies ($5x10^{10}$ pfu in 1 ml = 5 x 10^{10} pfu/ml), relatively little binding was observed by the Graph5-01 or wildtype clones to SWNT paste in the phage binding studies as shown in FIGURE 17. The differences in binding observed between these two experiments may be due to the manner in which the SWNT paste substrate was prepared and handled. The centrifugation of the wet, malleable SWNT paste used in the confocal experiments may have lead to trapping of both specific and nonspecific phage within the substrate, whereas the use of large dessicated SWNT aggregates in the phage binding studies may have prevented this. Wet paste was used in the confocal experiments to facilitate mounting under a coverslip, but future confocal binding experiments should utilize dessicated SWNT aggregates.

SWNT paste samples treated with peptides having sequences corresponding to the pIII inserts of the phage clones used above were also prepared but were not visualized.

Visualization of Phage on HOPG Using AFM

The binding of phage on carbon planchet and SWNT paste could not be analyzed using AFM due to the roughness of the substrate surfaces. Instead, HOPG was used and the results are shown in FIGURE 22. Phage clone Graph5-01 (specific for carbon planchet) could be observed to bind to HOPG, whereas the wildtype clone was not readily observed on HOPG.

The phage binding studies and the visualization of peptides and phage binding to carbon planchets by confocal microscopy in this example consistently showed that the sequences N'-WWSWHPW-C' (SEQ ID NO:238) and N'-HWSWWHP-C' (SEQ ID NO:239) bound with greatest efficiencies to carbon planchet. Phage binding studies also revealed that the phage clone Hipco12R44-01 (N'-DMPRTTMSPPPR-C') (SEQ ID NO:196) bound most efficiently to SWNT paste.

Little crossreactivity was observed in the phage binding studies and confocal experiments between the carbon planchet-specific phage clones and SWNT paste. Although the graphene structures present in the carbon planchets and SWNTs are theoretically very similar. It is possible that the walls of the SWNTs in the "raw" paste used in this studies contained contaminants and/or had been damaged by oxidation. To eliminate the possibility of the limited crossreactivity (i.e., high specificity) of the sequences due to the presence of possible contaminants, it may be desirable to use a purer nanotube source.

EXAMPLE IV. APPLICATIONS OF BIOLOGIC MATERIALS WITH AFFINITIES TO ELEMENTAL CARBON-CONTAINING MOLECULES

Examples illustrated below are illustrations of applications of the present invention, wherein SEQ ID NOS:1-245 may be used. In addition, examples may be applied using the methods and compositions of the present invention with other elemental carbon-containing molecules.

Separation Between Metallic and Semi-conducting CNT.

Current synthetic methods for producing single walled carbon nanotubes (SWNT) yield mixtures of metallic and semi-conducting SWNTs. In order to fabricate nanoscale electric devices, it is beneficial to separate the metallic SWNT and semi-conducting SWNT. Minute shape and symmetry differences between metallic and semi-conducting SWNT may be distinguished by the fast-evolved proteins obtained using the phage display or similar method. Based on the selected protein sequences from the phage display results, the negative column may be built to purify the mixture of metallic and semi-conducting SWNTs. If the mixture of metallic and semi-conducting SWNTs is passed through the negative column, the specific interaction between the peptides and one metallic or semi-conducting SWNTs cause the elution time difference. If metallic SWNTs binding peptides are applied to the negative column, the semi-conducting SWNTs elute faster than metallic SWNTs. Therefore, the one specific SWNT can be separated. A schematic diagram of SWNTs purifying negative column is shown in FIGURE 23.

Alignment of Carbon Nanotubes

One of the greatest challenges in using carbon nanotubes as nanoscale devices is aligning the nanotubes in three-dimensional arrays. Although a chemical vapor deposition (CVD) method may produce unique aligned structure from the fabrication, a CVD method may also produce a mixture of

metallic and semi-conducting SWNTs together. Because fabrication of the nano-electric devices is so precise, it is beneficial to separate the semi-conducting SWNTs from the mixture. The separation may be performed according to the method previously described. Although several approaches were used in this example such as LB-film method and meniscus force control, etc., these methods have produced only orientational aligned SWNT alignment. Both positionally and orientationally aligned SWNT 2D or 3D structures were built when phages having a specific binding property to SWNTs were used. SWNTs connected by phage as shown in FIGURE 24, behave like di-block copolymers which have two rigid block connected by the peptide unit. It is expected that SWNT connected phage building blocks would produce microphase-separated lamellar like structure, with the resulting structure having aligned SWNT structures.

SWNT to P-N Junction SWNT by Peptide Binding

Without any chemical modification, semi-conducting SWNTs generally may have an intrinsic p-type electric property. Chemical modification with an electron-donating group may convert the p-type SWNT to n-type SWNT. Periodically bound peptides that generally have separate negatively and positively charged protein domains may cause the electronic properties of SWNTs. SWNTs that have periodic positively and negatively charged domains may be identical structures with P-N junction semiconductor structures. It is possible that the interconnection of these P-N junctions cause FET and higher architecture of complicated integrated circuit functions as NAND, NOR, AND, OR gates. A schematic diagram of n-type SWNT modification using SWNT binding peptides is shown in FIGURE 25. These same modifications may be applied to multi-walled nanotubes and multi-walled nanotube pastes.

Solubility and Biocompatibility of Nanotubes

Low solubility in the solvent may block further application of SWNT. Generally, solubilization in water is essential for the biologic application of SWNT. Although wrapping polymers and surfactants were applied to solubilize the SWNT in this example, they must further be applied to biologic systems. It is believed that hydrophilic peptide groups conjugated with peptides that recognize the SWNT surfaces may solubilize the SWNT in water. In addition, removal of hydrophilic peptide groups may help SWNTs solubilize in non-polar solvents. These same modifications may be applied to multi-walled nanotubes and multi-walled nanotube pastes.

Wiring the Semi-Conducting SWNT

In accordance with the present invention, peptides recognizing SWNT's (metallic and semi conducting) may be wired together to form an integrated SWNT circuit and may serve as a functioning electric device. Similarly, the wiring technique may be applied to multi-walled nanotubes and other elemental carbon-containing molecules.

Biosensor

Biocompatible SWNTs may be utilized as a biosensor to detect minute chemical or physical changes in organisms. Conductivity of metallic SWNTs may generally be highly affected by the electron distribution around the SWNTs. As such, biologic interactions may be monitored by measuring the conductivity of SWNTs that are conjugated by two recognition moieties: one for SWNT and the other for the biologic targets. When the biologic target detecting-peptides bind with target molecules, the electron distribution in SWNTs may be affected by surrounding peptides. Binding and non-binding states of peptides may be monitored by electric signal and directly used as biosensors, such as antigen-antibody detection, glucose measurement in blood as well as others. Multi-walled nanotubes or other elemental carbon-containing molecules may also be used as biosensors using methods and compositions of the present invention.

Additionally, the peptide chain conformations that bind to SWNT are also affected by the pH, ionic strength, concentration of metal ion, and temperature changes. These environmental changes may also affect the electron distribution of SWNTs. All of these changes may be detected using SWNTs binding peptides.

8. Medication Release System

SWNTs may be used as robust scaffold to contain a drug. In addition, SWNTs may also be used to deliver a drug, especially if the SWNTs binding peptides are modified by the medications. For example, the medications connected by the peptides may slowly be released over time. Generally, these medications function similarly to patch-type medication delivery systems. A schematic diagram for the application of SWNT as a drug releasing system is shown in FIGURE 26. In addition, the medication may be directly implanted into the disease-site such as for example, a tumor cell.

Other elemental carbon-containing molecules may also be used as pharmaceutical compositions of the present invention that release drugs, diagnostic markers, and/or medications to be used with methods and compositions of the present invention for preventive or prophylactic therapy, as treatment, for diagnosis, monitoring, and/or for screening (e.g., of drugs, symptoms, interactions, and/or effects).

Cancer Medication

Biocompatible CNT may be used as radioactive or highly toxic medication delivery. In addition, multi-walled carbon nanotubes (MWNT) may be converted to biocompatible MWNT by peptides that have specific binding properties to MWNT. MWNTs generally contain at least about 3-4 nm of MWNT channel. This channel of MWNT may be filled by highly toxic or radioactive medications for special usage such as chemo-/radio- therapy. MWNTs that contain highly toxic or radioactive medication may then be directly implanted to the tumor cells or organism and thereafter, release the highly toxic or radioactive medication as desired. By changing the diameter of the inner channel, the releasing speed may be

controlled. A schematic diagram for the application of SWNTs in cancer medication is shown in FIGURE 27.

Other elemental carbon-containing molecules may also be used for the therapeutic delivery of agents as treatment tools or for monitoring disease progression (e.g., for cancer or other pathologic conditions).

The present invention may or may not include all the above-mentioned components. For example, biologic scaffolds of the present invention may be prepared in the absence of a substrate. In addition, the methods and compositions of the present invention may be applied for uses in fields such as optics, microelectronics, magnetics, and engineering. The applications include the synthesis of elemental carbon-containing materials, carbon nanutube alignment, creation of biologic semiconductors, junction conversion for single-walled nanotube paste, junction conversion for multi-walled nanotube paste, enhancing solubility and biologic compatability of single- and multi-walled nanotube paste, producing an integrated single- and multi-walled nanotube paste, biosensor production, release of pharmaceutical compositions, treatment of cancer, and combinations thereof.

While this invention has been described in reference to illustrative embodiments, this description is not intended to be construed in a limiting sense. Various modifications and combinations of the illustrative embodiments, as well as other embodiments of the invention will be apparent to persons skilled in the art upon reference to the description. It is therefore intended that the appended claims encompass any such modifications or embodiments.

CLAIMS

What is claimed is:

1. A method for directed semiconductor formation comprising the steps of:

contacting a polymeric organic material that binds a predetermined face specificity semiconductor material with a first ion to create a semiconductor material precursor; and

adding a second ion to the semiconductor material precursor, wherein the polymeric organic material directs formation of the predetermined face specificity semiconductor material.

2. The method of claim 1, wherein the polymeric organic material is an amino acid oligomer.

3. The method of claim 1, wherein the polymeric organic material is an amino acid oligomer on the surface of a bacteriophage.

4. The method of claim 1, wherein the polymeric organic material is an amino acid oligomer displayed on the surface of bacteria.

5. The method of claim 1, wherein the polymeric organic material is an amino acid oligomer displayed on the surface of cell as a label.

6. The method of claim 1, wherein the polymeric organic material is a nucleic acid oligomer.

7. The method of claim 1, wherein the polymeric organic material is a combinatorial library.

8. The method of claim 1, wherein the polymeric organic material comprises amino acid polymers of between about 7 and 20 amino acids.

9. The method of claim 1, wherein the predetermined face specificity semiconductor material is polycrystalline.

10. The method of claim 1, wherein the predetermined face specificity semiconductor material is single crystalline.

11. The method of claim 1, wherein the predetermined face specificity semiconductor material comprises a Group II-IV semiconductor material.

12. The method of claim 1, wherein the polymeric organic material comprises a chimeric protein.

13. The method of claim 1, wherein the polymeric organic material comprises a chimeric protein and wherein the portion of the chimeric protein that binds the semiconductor material is on the surface of the chimeric protein.

14. The method of claim 1, wherein the polymeric organic material comprises a chimeric protein and wherein the portion of the chimeric protein that binds the semiconductor material comprises between about 7 and 20 amino acids.

15. The method of claim 1, wherein the polymeric organic material nucleates size constrained crystalline semiconductor materials.

16. The method of claim 1, wherein the polymeric organic material controls the crystallographic phase of nucleated nanoparticles of the semiconductor.

17. The method of claim 1, wherein the polymeric organic material controls the aspect ratio of the nanocrystals of the semiconductor.

18. The method of claim 1, wherein the polymeric organic material controls the dopant levels of the semiconductor nanocrystals formed.

19. A method for directed semiconductor formation comprising the steps of:

contacting a peptide that binds a predetermined face specificity semiconductor material with a first ion to create a semiconductor material precursor; and

adding a second ion to the semiconductor material precursor, wherein the peptide directs formation of the predetermined face specificity semiconductor material.

20. The method of claim 19, wherein the peptide is on the surface of a bacteriophage.

21. The method of claim 19, wherein the peptide is part of a combinatorial library.

22. The method of claim 19, wherein the peptide comprises between about 7 and 20 amino acids.

23. The method of claim 19, wherein the predetermined face specificity semiconductor material is polycrystalline.

24. The method of claim 19, wherein the predetermined face specificity semiconductor material is single crystalline.

25. The method of claim 19, wherein the predetermined face specificity semiconductor material comprises a Group II-VI semiconductor material.

26. The method of claim 19, wherein the polymeric organic material is displayed on the surface of bacteria.

27. The method of claim 19, wherein the polymeric organic material is displayed on the surface of cell as a label.

28. The method of claim 19, wherein the peptide comprises a chimeric protein.

29. The method of claim 19, wherein the peptide comprises a chimeric protein and wherein the peptide portion of the chimeric protein that binds the semiconductor material is on the surface of the chimeric protein.

30. The method of claim 19, wherein the peptide comprises a chimeric protein and wherein the portion of the chimeric protein that binds the semiconductor material comprises between about 7 and 20 amino acids.

31. The method of claim 19, wherein the peptide nucleates size constrained crystalline semiconductor materials.

32. The method of claim 19, wherein the peptide controls the crystallographic phase of nucleated nanoparticles of the semiconductor.

33. The method of claim 19, wherein the peptide is selected from a 12 mer linear library.

34. The method of claim 19, wherein the peptide is selected from a 7 mer constrained library.

35. A method for nucleating semiconductor material comprising the steps of:

selecting a peptide that binds to a predetermined face specificity material;

preparing a portion of a gold surface that has been altered to have the peptide attached to the surface;

contacting the gold surface-peptide complex with a first ion needed for semiconductor crystal precursor formation; and

adding a second ions needed for semiconductor crystal formation.

36. The method of claim 35, wherein the peptide is selected from a constrained library.

37. The method of claim 35, wherein the gold-surface is prepared by forming a self-assembled monolayer with 2-mercaptoethylamine on the gold substrate.

38. The method of claim 35, wherein the predetermined face specificity semiconductor material comprises a Group II-VI semiconductor material.

39. The method of claim 35, wherein the semiconductor material is zinc sulfide and the solutions are zinc chloride and sodium sulfide.

40. The method of claim 35, wherein the semiconductor material is cadmium sulfide and the solutions are cadmium chloride and sodium sulfide.

41. The method of claim 35, wherein the peptide is selected by combinatorial library screening.

42. A method of constructing nanowires comprising the steps of:

selecting peptides that bind a predetermined face specificity semiconductor material; and

expressing the peptides as a fusion protein with a protein that is capable of self-assembly;

then interact fused with semiconductor precusors to direct formation of semiconductor nanocrystals.

43. The method of claim 42, wherein the peptides selected are expressed in high copy number.

44. The method of claim 42, wherein the self-assembled protein is on the surface of a bacteriophage.

45. The method of claim 42, wherein the polymeric organic material is displayed on the surface of bacteria.

46. The method of claim 42, wherein the polymeric organic material is displayed on the surface of cell as a label.

47. The method of claim 42, wherein the self-assembled protein comprises a portion of the major coat protein of M1 bacteriophage.

48. The method of claim 42, wherein the self-assembled protein comprises a portion of the p8 major coat protein of M1 bacteriophage.

49. A semiconductor made using the process of claim 1.

50. A semiconductor material made using the process of claim 15.

51. A nanowire made using the process of claim 35.

52. A biologic scaffold comprising:

a substrate capable of binding one or more biologic materials;

one or more biologic materials attached to the substrate; and

one or more elemental carbon-containing molecules attached to one or more biologic materials.

53. The biologic scaffold of claim 52, wherein the substrate is selected from the group consisting of silicon, Langmuir-Bodgett films, functionalized glass, germanium, ceramic, silicon, a semiconductor material, PTFE, carbon, polycarbonate, mica, mylar, plastic, quartz, polystyrene, gallium arsenide, gold, silver, metal, metal alloy, fabric, tissue, cell, organ, protein, antibody, and combinations thereof.

54. The biologic scaffold of claim 52, wherein the biologic material is selected from the group consisting of virus, bacteriophage, bacteria, peptide, protein, amino acid, steroid, drug, chromophore, antibody, enzyme, single-stranded

or double-stranded nucleic acid, nucleic acid polymer, and any chemical modifications thereof.

55. The biologic scaffold of claim 52, wherein the biologic material is identified by a combinatorial library screening.

56. The biologic scaffold of claim 52, wherein the biologic material is an amino acid oligomer present on the surface of a bacteriophage.

57. The biologic scaffold of claim 52, wherein the biologic material is an amino acid oligomer displayed on the surface of bacteria.

58. The biologic scaffold of claim 52, wherein the biologic material is an amino acid oligomer between 7 and 20 amino acids long.

59. The biologic scaffold of claim 52, wherein the biologic material is a peptide on the surface of a bacteriophage.

60. The biologic scaffold of claim 59, wherein the biologic material is a peptide selected from the group consisting of SEQ ID NO.:105-245.

61. The biologic scaffold of claim 52, wherein the elemental carbon-containing molecule recognizes a peptide selected from the group consisting of SEQ ID NO.:105-245.

62. The biologic scaffold of claim 52, wherein the elemental carbon-containing molecule is selected from the group consisting of $carbon_{60}$, carbon planchet, highly ordered pyrolytic graphite, single-walled nanotube paste, single-walled

nanotube, multi-walled nanotube, multi-walled nanotube paste, diamond, graphite, activated carbon, carbon black, industrial carbon, charcoal, coke, steel, carbon cycle, and combinations thereof.

63. The biologic scaffold of claim 52, wherein the substrate is absent from the biologic scaffold.

64. The biologic scaffold of claim 52, wherein the biologic scaffold is used for applications selected from the group consisting of synthesis of elemental carbon-containing materials, carbon nanutube alignment, creation of biologic semiconductors, junction conversion for single-walled nanotube paste, junction conversion for multi-walled nanotube paste, enhancing solubility and biologic compatability of single- and multi-walled nanotube paste, producing an integrated single- and multi-walled nanotube paste, biosensor production, release of pharmaceutical compositions, treatment of cancer, and combinations thereof.

65. A biologic scaffold comprising:

a substrate capable of binding one or more biologic materials;

a biologic material attached to the substrate and an organic polymer attached to the biologic material; and

one or more elemental carbon-containing molecules attached to the organic polymer.

66. The biologic scaffold of claim 65, wherein the substrate is selected from the group consisting of silicon, Langmuir-Bodgett films, functionalized glass, germanium,

ceramic, silicon, a semiconductor material, PTFE, carbon, polycarbonate, mica, mylar, plastic, quartz, polystyrene, gallium arsenide, gold, silver, metal, metal alloy, fabric, tissue, cell, organ, protein, antibody, and combinations thereof.

67. The biologic scaffold of claim 65, wherein the biologic material is selected from the group consisting of virus, bacteriophage, bacteria, peptide, protein, amino acid, steroid, drug, chromophore, antibody, enzyme, single-stranded or double-stranded nucleic acid, nucleic acid polymer, and any chemical modifications thereof.

68. The biologic scaffold of claim 65, wherein the biologic material and organic polymer are the same.

69. The biologic scaffold of claim 65, wherein the organic polymer is a protein, antibody, peptide, nucleic acid, chimeric molecule, drug, label, other carbon-containing organic materials known to exist in eukaryotic organisms, and derivatives or analogs of biologic polymers that contain one or more biologic monomers in combinations with synthetic monomers that mimic those found naturally.

70. The biologic scaffold of claim 65, wherein the organic polymer is identified by a combinatorial library screening.

71. The biologic scaffold of claim 65, wherein the organic polymer is an amino acid oligomer between 7 and 20 amino acids long.

72. The biologic scaffold of claim 65, wherein the organic polymer is a peptide that recognizes a select portion of the biologic material

73. The biologic scaffold of claim 65, wherein the second biologic material is a peptide selected from the group consisting of SEQ ID NO.: 105-245.

74. The biologic scaffold of claim 65, wherein the elemental carbon-containing molecule recognizes a peptide selected from the group consisting of SEQ ID NO.:105-245.

75. The biologic scaffold of claim 65, wherein the elemental carbon-containing molecule is selected from the group consisting of $carbon_{60}$, carbon planchet, highly ordered pyrolytic graphite, single-walled nanotube paste, single-walled nanotube, multi-walled nanotube, multi-walled nanotube paste, diamond, graphite, activated carbon, carbon black, industrial carbon, charcoal, coke, steel, carbon cycle, and combinations thereof.

76. The biologic scaffold of claim 65, wherein the biologic scaffold is used for applications selected from the group consisting of synthesis of elemental carbon-containing materials, carbon nanutube alignment, creation of biologic semiconductors, junction conversion for single-walled nanotube paste, junction conversion for multi-walled nanotube paste, enhancing solubility and biologic compatability of single- and multi-walled nanotube paste, producing an integrated single- and multi-walled nanotube paste, biosensor production, release of pharmaceutical compositions, treatment of cancer, and combinations thereof.

77. The biologic scaffold of claim 65, wherein the substrate and the biologic material are the same.

78. A biologic scaffold comprising:

a substrate capable of binding one or more bacteriophages;

one or more bacteriophages attached to the substrate;

one or more peptides that recognize a portion of the bacteriophage; and

one or more elemental carbon-containing molecules that recognize the peptide.

79. The biologic scaffold of claim 78, wherein the substrate is silicon, Langmuir-Bodgett films, functionalized glass, germanium, ceramic, silicon, a semiconductor material, PTFE, carbon, polycarbonate, mica, mylar, plastic, quartz, polystyrene, gallium arsenide, gold, silver, metal, metal alloy, fabric, tissue, cell, organ, protein, antibody, and combinations thereof.

80. The biologic scaffold of claim 78, wherein the peptide is selected from the group consisting of SEQ ID NO.:105-245.

81. The biologic scaffold of claim 78, wherein the elemental carbon-containing molecule is selected from the group consisting of $carbon_{60}$, carbon planchet, highly ordered pyrolytic graphite, single-walled nanotube paste, single-walled nanotube, multi-walled nanotube, multi-walled nanotube paste, diamond, graphite, activated carbon, carbon black,

industrial carbon, charcoal, coke, steel, carbon cycle, and combinations thereof.

82. The biologic scaffold of claim 78, wherein the peptide is selected from the group consisting of drug, antibody, chromophore, light-emitting label, light absorbing label, and organic polymer.

83. The biologic scaffold of claim 78, wherein the substrate is absent.

84. A method of making a biologic scaffold comprising:

providing a substrate capable of binding one or more biologic materials;

attaching one or more biologic materials to the substrate; and

contacting one or more elemental carbon-containing molecules with the biologic material to form a biologic scaffold.

85. The method of claim 84, wherein the substrate is selected from the group consisting of silicon, Langmuir-Bodgett films, functionalized glass, germanium, ceramic, silicon, a semiconductor material, PTFE, carbon, polycarbonate, mica, mylar, plastic, quartz, polystyrene, gallium arsenide, gold, silver, metal, metal alloy, fabric, tissue, cell, organ, protein, antibody, and combinations thereof.

86. The method of claim 84, wherein the biologic material is selected from the group consisting of virus, bacteriophage, bacteria, peptide, protein, amino acid,

steroid, drug, chromophore, label, antibody, enzyme, single-stranded or double-stranded nucleic acid, nucleic acid polymer, chimeric molecule, drug, any other carbon-containing materials known to exist in eukaryotic organisms, and derivatives or analogs of biologic polymers that contain one or more biologic monomers in combination with synthetic monomers that mimic those found naturally.

87. The method of claim 84, wherein the biologic material is identified by combinatorial library screening.

88. The method of claim 84, wherein the biologic material is an amino acid oligomer on the surface of a bacteriophage.

89. The method of claim 84, wherein the biologic material is a peptide displayed on the surface of bacteria.

90. The method of claim 88, wherein the amino acid oligomer is between 7 and 20 amino acids long.

91. The method of claim 89, wherein the peptide is selected from the group consisting of SEQ ID NO.:105-245.

92. The method of claim 89, wherein the peptide is selected from the group consisting of drug, antibody, chromophore, light-emitting label, light absorbing label, and organic polymer.

93. The method of claim 84, wherein the elemental carbon-containing molecule recognizes a peptide selected from the group consisting of SEQ ID NO.:105-245.

94. The method of claim 84, wherein the elemental carbon-containing molecule is selected from the group

consisting of carbon$_{60}$, carbon planchet, highly ordered pyrolytic graphite, single-walled nanotube paste, single-walled nanotube, multi-walled nanotube, multi-walled nanotube paste, diamond, graphite, activated carbon, carbon black, industrial carbon, charcoal, coke, steel, carbon cycle, and combinations thereof.

95. The method of claim 84, wherein providing a substrate capable of binding one or more biologic materials and attaching one or more biologic materials to the substrate are not required to make the biologic scaffold.

96. A molecule comprising:

an organic polymer, wherein the organic polymer selectively recognizes an elemental carbon-containing molecule.

97. The molecule of claim 96, wherein the molecule is used for applications selected from the group consisting of synthesis of elemental carbon-containing materials, carbon nanutube alignment, creation of biologic semiconductors, junction conversion for single-walled nanotube paste, junction conversion for multi-walled nanotube paste, enhancing solubility and biologic compatability of single- and multi-walled nanotube paste, producing an integrated single- and multi-walled nanotube paste, biosensor production, release of pharmaceutical compositions, treatment of cancer, and combinations thereof.

98. The molecule of claim 96, wherein the organic polymer is a nucleic acid oligomer.

99. The molecule of claim 96, wherein the organic polymer is selected by a combinatorial library screening.

100. The molecule of claim 96, wherein the organic polymer is an amino acid oligomer on the surface of a bacteriophage.

101. The molecule of claim 100, wherein the amino acid oligomer is displayed on the surface of bacteria.

102. The molecule of claim 100, wherein the amino acid oligomer is between 7 and 15 amino acids long.

103. The molecule of claim 96, wherein the organic polymer is a peptide on the surface of a bacteriophage.

104. The molecule of claim 103, wherein the peptide is selected from the group consisting of SEQ ID NO.:105-245.

105. The molecule of claim 96, wherein the elemental carbon-containing molecule recognizes a peptide selected from the group consisting of SEQ ID NO.:105-245.

106. The molecule of claim 96, wherein the elemental carbon-containing molecule is selected from the group consisting of $carbon_{60}$, carbon planchet, highly ordered pyrolytic graphite, single-walled nanotube paste, single-walled nanotube, multi-walled nanotube, multi-walled nanotube paste, diamond, graphite, activated carbon, carbon black, industrial carbon, charcoal, coke, steel, carbon cycle, and combinations thereof.

107. An integrated circuit derived from the biologic scaffold of claim 52.

108. A biosensor derived from the biologic scaffold of claim 52.

109. A drug delivery system using the biologic scaffold of claim 52.

110. A pharmaceutical composition using a pharmaceutically effective amount of the molecule of claim 96.

111. A treatment for cancer using the biologic scaffold of claim 52.

112. A method for separating metallic and semi-conducting nanotubes comprising the steps of:

obtaining protein sequences using a combinatorial library screening that distinguishes metallic and semi-conducting nanotubes;

contacting a mixture of metallic and semi-conducting nanotubes with the obtained protein sequences; and

separating the semi-conducting nanotube from the metallic nanotube

113. The method of claim 112, wherein metallic and semi-conducting nanotubes are selected from the group consisting of single-walled nanotubes and multi-walled nanotubes.

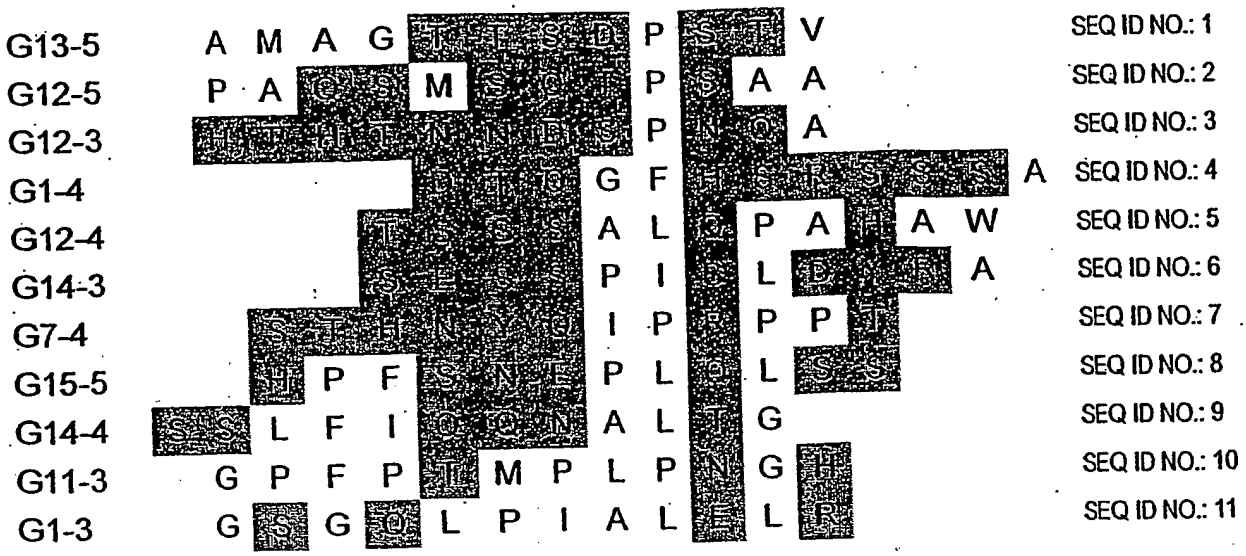

G13-5
G12-5
G12-3
G1-4
G12-4
G14-3
G7-4
G15-5
G14-4
G11-3
G1-3
SEQ ID NO.: 1
SEQ ID NO.: 2
SEQ ID NO.: 3
SEQ ID NO.: 4
SEQ ID NO.: 5
SEQ ID NO.: 6
SEQ ID NO.: 7
SEQ ID NO.: 8
SEQ ID NO.: 9
SEQ ID NO.: 10
SEQ ID NO.: 11

Fig. 1

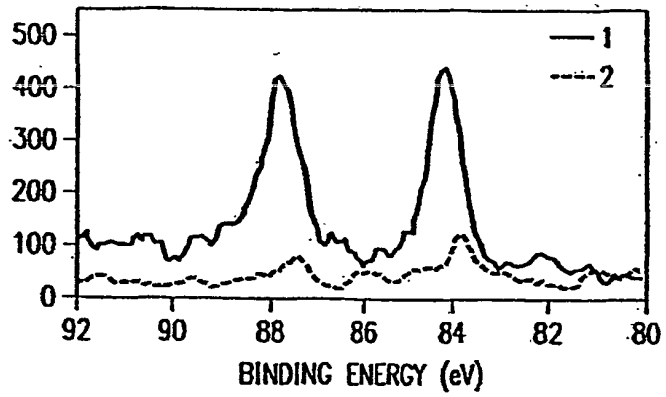


FIG. 2A

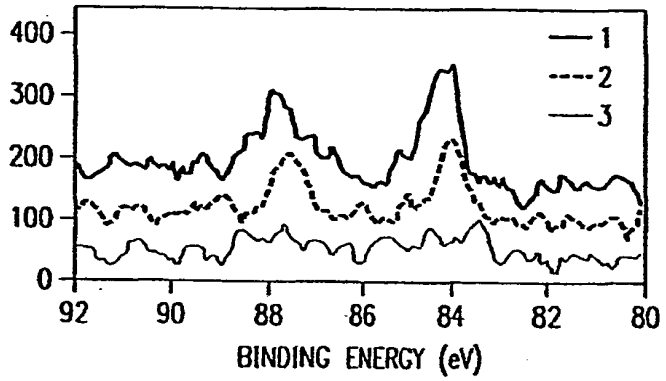


FIG. 2B

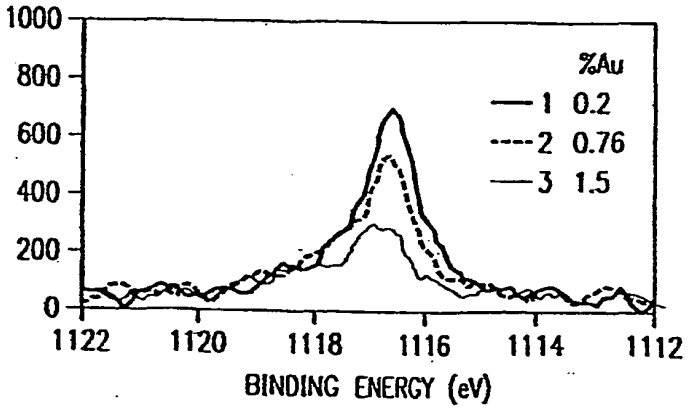


FIG. 2C

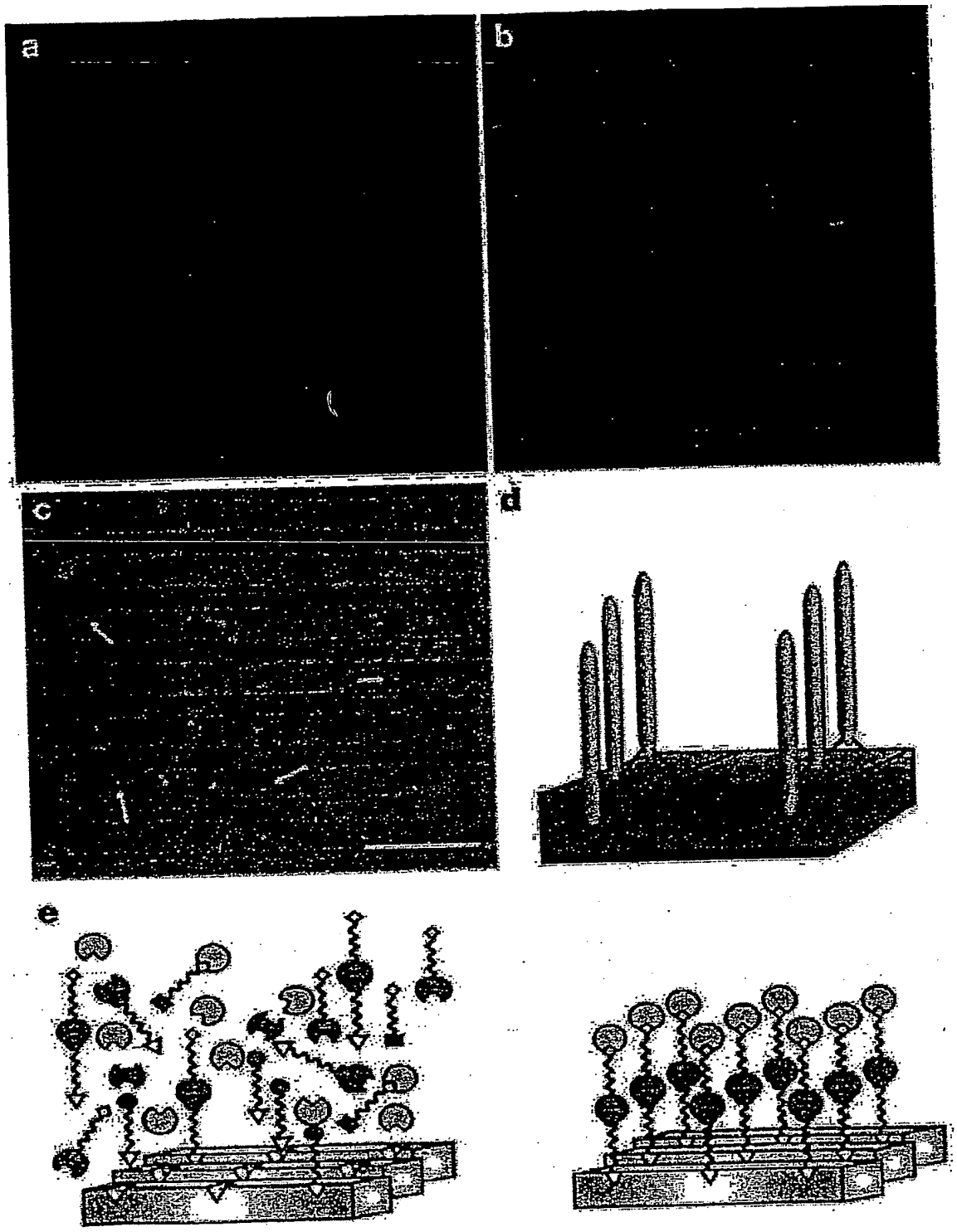


Fig. 3

Single Crystal

er library (N to C terminus)

CEF-81	E1	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-82	E2	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-83	E3	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-84	E4	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-85	E5	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-86	E6	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-88	E8	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-89	E9	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-90	E10	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-91	E11	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-92	E12	C	H	A	S	N	R	L	S	C			SEQ ID NO.:12
CEF-159	E13	S	M	D	R	S	D	M	T	M	R	L	P	SEQ ID NO.:13
CEF-160	E14	G	T	F	T	P	R	P	T	P	I	Y	P	SEQ ID NO.:14
CEF-161	E15	Q	M	S	E	N	L	T	S	Q	I	E	S	SEQ ID NO.:15
CEF-162	E16	D	M	L	A	R	L	R	A	T	A	G	P	SEQ ID NO.:16
CEF-163	E18	S	Q	T	W	L	L	M	S	P	V	A	T	SEQ ID NO.:17
CEF-164	E19	A	S	P	D	Q	Q	V	G	P	L	Y	V	SEQ ID NO.:18
CEF-165	E20	L	T	W	S	P	L	Q	T	V	A	R	F	SEQ ID NO.:19
CEF-166	E21	Q	I	S	A	H	Q	M	P	S	R	P	I	SEQ ID NO.:20
CEF-167	E22	S	M	K	Y	N	L	I	V	D	S	P	Y	SEQ ID NO.:21
CEF-168	E23	wt												
CEF-169	E24	Q	M	P	I	R	N	Q	L	A	W	P	M	SEQ ID NO.:22
CEF-170	E25	T	Q	N	L	E	I	R	E	P	L	T	P	SEQ ID NO.:23
CEF-171	E26	Q	I	S	A	H	Q	M	P	S	R	P	I	SEQ ID NO.:20
CEF-172	E27	Y	P	M	S	P	S	P	Y	P	Y	Q	L	SEQ ID NO.:24
CEF-173	E28	S	F	M	I	Q	P	T	P	L	P	P	S	SEQ ID NO.:25
CEF-174	E29	G	L	A	P	H	I	H	S	L	N	E	A	SEQ ID NO.:26
CEF-175	E30	M	Q	F	P	V	T	P	Y	L	N	A	S	SEQ ID NO.:27

Fig. 4

CdS Biopan 3 Sequences (N to C terminus)

JCW-96	S	P	G	D	S	L	K	K	L	A	A	S
JCW-97	S	P	G	D	S	L	K	K	L	A	A	S
JCW-98	Q	I	S	A	H	Q	M	P	S	R	P	I
JCW-99	S	P	G	D	S	L	K	K	L	A	A	S
JCW-100	S	P	G	D	S	L	K	K	L	A	A	S
JCW-101	S	P	G	D	S	L	K	K	L	A	A	S
JCW-102	S	P	G	D	S	L	K	K	L	A	A	S
JCW-103	S	P	G	D	S	L	K	K	L	A	A	S
JCW-104	S	P	G	D	S	L	K	K	L	A	A	S
JCW-105	G	Y	H	M	Q	T	L	P	G	P	V	A

SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:20
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:29

CdS Biopan 4 Sequences (N to C terminus)

JCW-106	S	L	T	P	L	T	T	S	H	L	R	S
JCW-108	S	L	T	P	L	T	T	S	H	L	R	S
JCW-111	S	L	T	P	L	T	T	S	H	L	R	S

SEQ ID NO.:30
SEQ ID NO.:30
SEQ ID NO.:30

CdS Biopan 5 Sequences (N to C terminus)

JCW-118	T	L	T	N	G	P	L	R	P	F	T	G
JCW-122	S	L	T	P	L	T	T	S	H	L	R	S

SEQ ID NO.:31
SEQ ID NO.:30

CdS Biopan 3 Sequences (repeat; N to C terminus))

JCW-125	S	P	G	D	S	L	K	K	L	A	A	S
JCW-126	S	P	G	D	S	L	K	K	L	A	A	S
JCW-127	S	P	G	D	S	L	K	K	L	A	A	S
JCW-128	S	P	G	D	S	L	K	K	L	A	A	S
JCW-129	S	P	G	D	S	L	K	K	L	A	A	S
JCW-130	S	L	T	P	L	T	T	S	H	L	R	S
JCW-131	S	P	G	D	S	L	K	K	L	A	A	S

SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:28
SEQ ID NO.:30
SEQ ID NO.:28

JCW-132 WT

JCW-133	S	P	G	D	S	L	K	K	L	A	A	S
JCW-134	S	P	G	D	S	L	K	K	L	A	A	S

SEQ ID NO.:28
SEQ ID NO.:28

CdS Biopan 2 Sequences (N to C terminus)

JCW-137	S	L	T	P	L	T	T	S	H	L	R	S
JCW-139	S	L	T	P	L	T	T	S	H	L	R	S
JCW-140	S	L	T	P	L	T	T	S	H	L	R	S
JCW-141	S	L	T	P	L	T	T	S	H	L	R	S

SEQ ID NO.:30
SEQ ID NO.:30
SEQ ID NO.:30
SEQ ID NO.:30

CdS Biopan 5 Sequences (repeat; N to C terminus)

JCW-146	T	L	T	N	G	P	L	R	P	F	T	G
JCW-148	L	N	T	P	K	P	F	T	L	G	Q	N

SEQ ID NO.:31
SEQ ID NO.:32

Fig. 5

Other arrangements (N to C terminus)

4	B71	CEF-215	C	D	L	Q	N	Y	K	A	C	SEQ ID NO.:33
4	G	CEF-156	C	R	H	P	H	T	R	L	C	SEQ ID NO.:34
3t	H13	CEF-131	C	A	N	L	K	P	K	A	C	SEQ ID NO.:35
3t	H15	CEF-133	C	Y	I	N	P	P	K	V	C	SEQ ID NO.:36
3t	H14	CEF-132	C	N	N	K	V	P	V	L	C	SEQ ID NO.:37
3	B49	CEF-203	C	H	A	S	K	T	P	L	C	SEQ ID NO.:38
3t	H2	CEF-120	C	A	S	Q	L	Y	P	A	C	SEQ ID NO.:39
3	G4	CEF-102	C	N	M	T	Q	Y	P	A	C	SEQ ID NO.:40
3t	H17	CEF-135	C	F	A	P	S	G	P	A	C	SEQ ID NO.:41
4		B20	C	P	V	W	I	Q	A	P	C	SEQ ID NO.:42
5	CEF-27	B29	C	Q	V	A	V	N	P	L	C	SEQ ID NO.:43
3	G2	CEF-100	C	Q	P	E	A	M	P	A	C	SEQ ID NO.:44
3	B48	CEF-202	C	H	P	T	M	P	L	A	C	SEQ ID NO.:45
3a	B92	CEF-229	C	P	P	F	A	A	P	I	C	SEQ ID NO.:46

his-met-pro sequences from Aldrich ZnS screenings

3a	B63	CEF-207	C	N	K	H	Q	P	M	H	C	SEQ ID NO.:47
4		B18	C	F	P	M	R	S	N	Q	C	SEQ ID NO.:48
4a	B73	CEF-217	C	Q	S	M	P	H	N	R	C	SEQ ID NO.:49
5		B7	C	N	N	P	M	H	Q	N	C	SEQ ID NO.:50
5	CEF-28	B30	C	Q	S	M	P	H	N	R	C	SEQ ID NO.:49
5	CEF-34	B36	C	H	M	A	P	R	W	Q	C	SEQ ID NO.:51
5	CEF-35	B37	C	Q	S	M	P	H	N	R	C	SEQ ID NO.:49
	JCW-87	503	H	V	H	I	H	S	R	P	M	SEQ ID NO.:52
	JCW-87	503	H	V	H	I	H	S	R	P	M	SEQ ID NO.:52
5	JCW-65	5H7	L	P	N	M	H	P	L	P	L	SEQ ID NO.:53
4	JCW-57	4H9	L	P	L	R	L	P	P	M	P	SEQ ID NO.:54
4	JCW-30	437-10	H	S	M	I	G	T	P	T	T	SEQ ID NO.:55
4	JCW-28	437-8	S	V	S	V	G	M	K	P	S	SEQ ID NO.:56
4	JCW-21	437-1	L	D	A	S	F	M	Q	D	W	SEQ ID NO.:57
4	JCW-22	437-2	T	P	P	S	Y	Q	M	A	M	SEQ ID NO.:58
4	JCW-23	437-3	Y	P	Q	L	V	S	M	S	T	SEQ ID NO.:59
3	JCW-3	337-3	G	Y	S	T	I	N	M	Y	S	SEQ ID NO.:60
5	CEF-11	Z35	S	V	S	V	G	M	K	P	S	SEQ ID NO.:56
5	CEF-6	Z30	D	R	M	L	L	P	F	N	L	SEQ ID NO.:61
5	CEF-3	Z27	I	P	M	T	P	S	Y	D	S	SEQ ID NO.:62
5		Z22	M	Y	S	P	R	P	P	A	L	SEQ ID NO.:63
5		Z23	Q	P	T	T	D	L	M	A	H	SEQ ID NO.:64
5		Z15	A	T	H	V	Q	M	A	W	A	SEQ ID NO.:65
5		Z9	S	M	H	A	T	L	T	P	M	SEQ ID NO.:66
5		Z10	S	G	P	A	H	G	M	F	A	SEQ ID NO.:67
2		Z4	I	A	N	R	P	Y	S	A	Q	SEQ ID NO.:68
		C16	V	M	T	Q	P	T	R			SEQ ID NO.:69
		C10	H	M	R	P	L	S	I			SEQ ID NO.:70

Fig. 6

ZnS capping:		BP5	L	T	R	S	P	L	H	V	D	Q	R	R	SEQ ID NO.:71
		Z6	V	I	S	N	H	A	E	S	S	R	R	L	SEQ ID NO.:72
		Z8	S	G	P	A	H	G	M	F	A	R	P	L	SEQ ID NO.:67
		Z10													
ZnS 12-mer repeats															
5	JCW-44	537-4	S	V	S	V	G	M	K	P	S	P	R	P	SEQ ID NO.:56
4	JCW-28	437-8	S	V	S	V	G	M	K	P	S	P	R	P	SEQ ID NO.:56
5	CEF-11	Z35	S	V	S	V	G	M	K	P	S	P	R	P	SEQ ID NO.:56
CdS contamination															
1	CEF-83	E3	C	H	A	S	N	R	L	S	C				SEQ ID NO.: 12
PbS 7-mer repeats 7C															
4a	JCW-72	P74-4	H	T	H	I	P	N	Q						SEQ ID NO.:73
4	JCW-74	P74-6	H	T	H	I	P	N	Q						SEQ ID NO.:73
5	JCW-76	P75-2	L	A	P	V	S	P	P						SEQ ID NO.:74
5	JCW-78	P75-4	L	A	P	V	S	P	P						SEQ ID NO.:74
7C repeats															
	B73	CEF-217	C	Q	S	M	P	H	N	R	C				SEQ ID NO.:49
5	CEF-35	B37	C	Q	S	M	P	H	N	R	C				SEQ ID NO.:49
5	CEF-28	B30	C	Q	S	M	P	H	N	R	C				SEQ ID NO.:49
3t	G5	CEF-103	C	M	T	A	G	K	N	T	C				SEQ ID NO.:75
3t	G7	CEF-105	C	Q	T	L	W	R	N	S	C				SEQ ID NO.:76
3a	B93	CEF-230	C	T	S	V	H	T	N	T	C				SEQ ID NO.:77
5	CEF-30	B32	C	T	S	V	H	T	N	T	C				SEQ ID NO.:77
4a	B72	CEF-216	C	P	S	L	A	M	N	S	C				SEQ ID NO.:78
5	CEF-23	B25	C	P	S	L	A	M	N	S	C				SEQ ID NO.:78
5	CEF-33	B35	C	S	N	N	T	V	H	A	C				SEQ ID NO.:79
5	CEF-25	B27	C	S	N	N	T	V	H	A	C				SEQ ID NO.:79
5	CEF-37	B39	C	L	P	A	Q	G	H	V	C				SEQ ID NO.:80
5	CEF-29	B31	C	L	P	A	Q	V	H	V	C				SEQ ID NO.:81
5	CEF-22	B24	C	L	P	A	Q	G	H	V	C				SEQ ID NO.:80
3a	B96	CEF-234	C	P	P	K	N	V	R	L	C				SEQ ID NO.:82
4	G	CEF-158	C	P	H	I	N	A	H	A	C				SEQ ID NO.:83
4	G	CEF-149	C	I	V	N	L	A	R	A	C				SEQ ID NO.:84

Fig. 7

Biopan 4 Lead Sulfide

JCW-154	T	M	G	F	T	A	P	R	F	P	H	Y	SEQ ID NO.:85
JCW-155	A	T	Q	S	Y	V	R	H	P	S	L	G	SEQ ID NO.:86
JCW-156	T	S	T	T	Q	G	A	L	A	Y	L	F	SEQ ID NO.:87
JCW-157	D	P	P	W	S	A	I	V	R	H	R	D	SEQ ID NO.:88
JCW-158	F	D	N	K	P	F	L	R	V	A	S	E	SEQ ID NO.:89
JCW-159	H	Q	S	H	T	Q	Q	N	K	R	H	L	SEQ ID NO.:90
JCW-160	T	S	T	T	Q	G	A	L	A	Y	L	F	SEQ ID NO.:91
JCW-161	K	T	P	I	H	T	S	A	W	E	F	Q	SEQ ID NO.:92
JCW-162	D	P	P	W	S	A	I	V	R	H	R	D	SEQ ID NO.:88
JCW-163	T	M	G	F	T	A	P	R	F	R	H	Y	SEQ ID NO.:85

Biopan 5 Lead Sulfide

JCW-164	T	M	G	F	T	A	P	R	F	P	H	Y	SEQ ID NO.:85
JCW-165	T	M	G	F	T	A	P	R	F	P	H	Y	SEQ ID NO.:85
JCW-166	D	L	F	H	L	K	P	V	S	N	E	K	SEQ ID NO.:93
JCW-167	T	M	G	F	T	A	P	R	F	P	H	Y	SEQ ID NO.:85
JCW-168	D	P	P	W	S	A	I	V	R	H	R	D	SEQ ID NO.:88
JCW-169	K	P	F	W	T	S	S	P	D	V	M	T	SEQ ID NO.:94
JCW-170	D	P	P	W	S	A	I	V	R	H	R	D	SEQ ID NO.:88
JCW-171	P	W	A	A	T	S	K	P	P	Y	S	S	SEQ ID NO.:95
JCW-172	T	M	G	F	T	A	P	R	F	P	H	Y	SEQ ID NO.:85
JCW-173	T	M	G	F	T	A	P	R	F	P	H	Y	SEQ ID NO.:85

Fig. 8

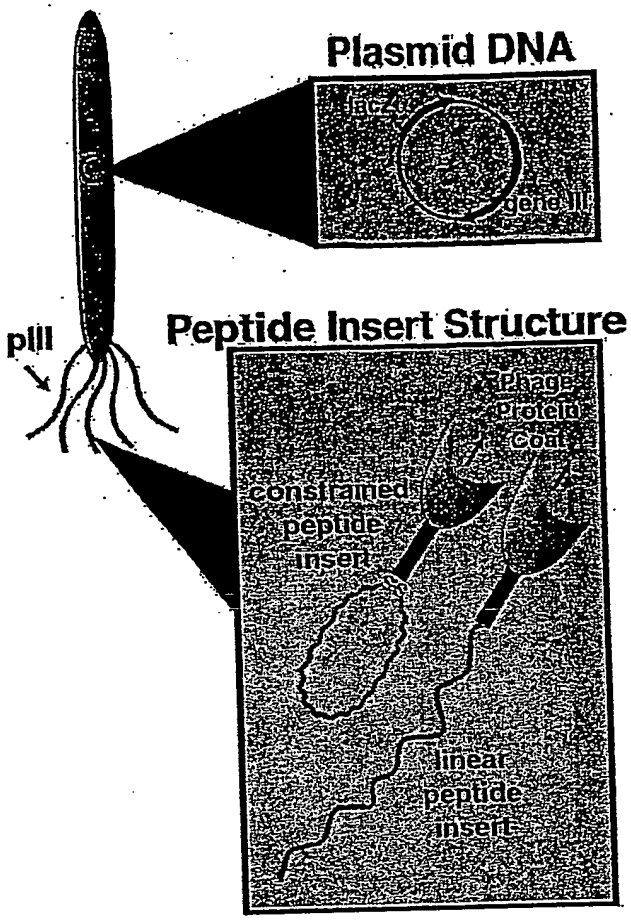

Plasmid DNA
lacZ
gene III
pIII
Peptide Insert Structure
phage protein coat
constrained peptide insert
linear peptide insert

Fig. 9

THIRD ROUND % amino acid occurrence by position

Amino Acid functionality	pos 1	pos 2	pos 3	pos 4	pos 5	pos 6	pos 7
(+) Charges	20	5.882	22.86	5.714	11.43	25.71	25.71
(-) Charges	2.857	2.941	8.571	0	5.714	2.857	2.857
Phobics	14.29	20.59	17.14	28.57	22.86	28.57	20
OH	25.71	38.24	22.86	14.29	28.57	14.29	37.14
Met	2.857	5.882	0	5.714	2.857	2.857	5.714
Trp, Phe	2.857	0	8.571	11.43	0	0	2.857
Pro	11.43	20.59	14.29	11.43	17.14	14.29	2.857
Asn, Gln	20	5.882	5.714	22.86	11.43	11.43	2.857

FOURTH ROUND

Amino Acid functionality	pos 1	pos 2	pos 3	pos 4	pos 5	pos 6	pos 7
(+) Charges	9.091	27.27	4.545	23.81	28.57	40.91	9.524
(-) Charges	4.545	0	0	0	0	0	0
Phobics	13.64	36.36	31.82	47.62	28.57	9.091	38.1
OH	9.091	22.73	18.18	0	14.29	9.091	19.05
Met	0	0	9.091	9.524	9.524	4.545	0
Trp, Phe	4.545	0	4.545	0	0	0	0
Pro	22.73	13.64	4.545	9.524	9.524	9.091	9.524
Asn, Gln	36.36	0	27.27	9.524	9.524	27.27	23.81

Fig. 10

FIFTH ROUND

Amino Acid	pos 1	pos 2	pos 3	pos 4	pos 5	pos 6	pos 7
(+) Charges	7.407	3.704	3.704	3.704	48.15	26.92	14.81
(-) Charges	0	3.704	0	0	0	0	0
Phobics	14.81	7.407	29.63	7.407	25.93	3.846	25.93
OH	22.22	18.52	11.11	11.11	11.11	3.846	18.52
Met	0	3.704	7.407	37.04	3.704	0	3.704
Trp, Phe	0	0	3.704	3.704	0	3.846	3.704
Pro	3.704	11.11	37.04	18.52	0	3.846	0
Asn, Gln	51.85	51.85	7.407	18.52	11.11	57.69	33.33

3rd

C	N	K	H	Q	P	M	H	C	SEQ ID NO.:47
C	Q	N	P	M	Q	T	F	C	SEQ ID NO.:96
C	N	Q	L	S	T	R	P	C	SEQ ID NO.:97
C	N	N	K	V	P	V	L	C	SEQ ID NO.:37
C	L	Q	N	R	Q	S	Q	C	SEQ ID NO.:98
C	Q	L	Q	R	Q	W	N	C	SEQ ID NO.:99
C	Q	V	N	S	A	H	Q	C	SEQ ID NO.:100

4th

C	Q	S	M	P	H	N	R	C	SEQ ID NO.:49
C	F	P	M	R	S	N	Q	C	SEQ ID NO.:101
C	P	P	Q	P	N	R	Q	C	SEQ ID NO.:102
C	Q	M	P	M	Q	H	N	C	SEQ ID NO.:103
C	A	N	V	A	Q	R	N	C	SEQ ID NO.:104

5th

A7 → clone

C	H	M	A	P	R	W	Q	C	SEQ ID NO.:51
C	Q	S	M	P	H	N	R	C	SEQ ID NO.:49
C	Q	S	M	P	H	N	R	C	SEQ ID NO.:49
C	N	N	P	M	H	Q	N	C	SEQ ID NO.:50
C	N	N	P	M	H	Q	N	C	SEQ ID NO.:50
C	N	N	P	M	H	Q	N	C	SEQ ID NO.:50

Fig. 11

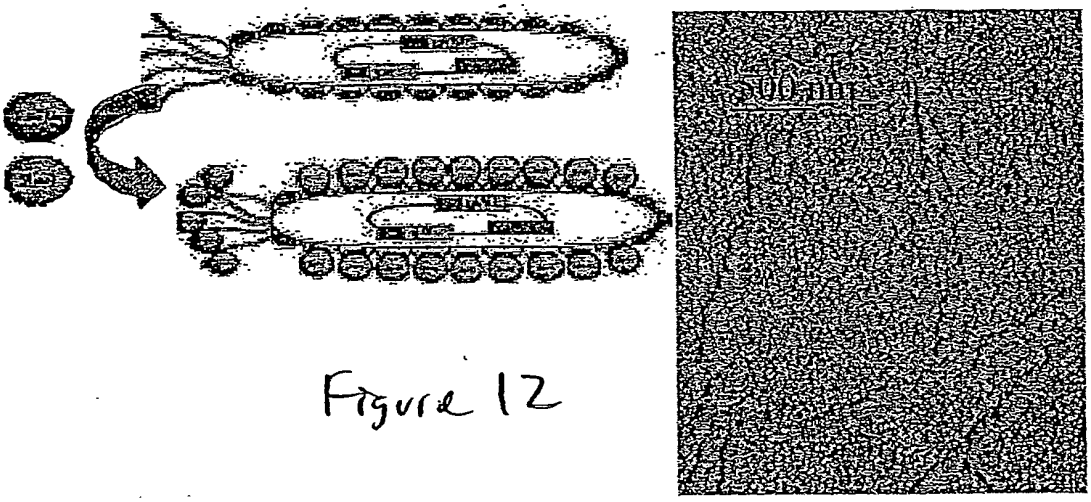


Figure 12

Round 3 – 1st try		
Graph3-07	SEQ ID NO:105	CNNKQLYYC
Graph3-01	SEQ ID NO:106	CQTAWIGQC
Graph3-08	SEQ ID NO:107	CQSANKLTC
Graph3-02	SEQ ID NO:108	CIPYTMAMC
Graph3-03	SEQ ID NO:109	CLPSYHNNC
Graph3-06	SEQ ID NO:110	CVSVAHKDC
Graph3-05	SEQ ID NO:111	CEVTTLYRC
Graph3-09	SEQ ID NO:112	CELTAFPAC
Graph3-04	SEQ ID NO:113	CTLASPHQC
Graph3-10	SEQ ID NO:114	CPLTGGPTC

Round 4 – 1st try		
Graph4-04	SEQ ID NO:115	CWWSWHPWC
Graph4-05	SEQ ID NO:115	CWWSWHPWC
Graph4-12	SEQ ID NO:115	CWWSWHPWC
Graph4-17	SEQ ID NO:115	CWWSWHPWC
Graph4-19	SEQ ID NO:115	CWWSWHPWC
Graph4-06	SEQ ID NO:116	CQKSGVHLC
Graph4-07	SEQ ID NO:117	CLFNALIRC
Graph4-20	SEQ ID NO:118	CVMWTSHSC
Graph4-09	SEQ ID NO:119	CVSRWRASC
Graph4-10	SEQ ID NO:120	CSSWEPKSC
Graph4-11	SEQ ID NO:121	CTLTGPFAC
Graph4-13	SEQ ID NO:122	CPPVLGNLC
Graph4-03	SEQ ID NO:123	CPHAPSGPC
Graph4-15	SEQ ID NO:124	CPLHKNGKC
Graph4-02	SEQ ID NO:125	CRSHHSWSC
Graph4-16	SEQ ID NO:126	CKQFLSLSC
Graph4-14	SEQ ID NO:127	CDDASLRHC
Graph4-08	SEQ ID NO:128	CDNRGSQFC

Round 4 – 2nd try		
Graph43-10	SEQ ID NO:133	CYFSWWHPC
Graph43-16	SEQ ID NO:133	CYFSWWHPC
Graph43-06	SEQ ID NO:134	CSPVKYPSC
Graph43-08	SEQ ID NO:135	CTSHFKLHC
Graph43-01	SEQ ID NO:136	CQQGTAPLC
Graph43-02	SEQ ID NO:137	CQEHSAKSC
Graph43-18	SEQ ID NO:138	CQTEDLPRC
Graph43-07	SEQ ID NO:139	CNRTSPAHC
Graph43-15	SEQ ID NO:140	CQGNHIGLC
Graph43-09	SEQ ID NO:141	CLNNYTHTC
Graph43-20	SEQ ID NO:142	CLTTASTKC
Graph43-12	SEQ ID NO:143	CLLSLRPAC
Graph43-04	SEQ ID NO:144	CDSQLWPIC
Graph43-05	SEQ ID NO:145	CDDRTTKIC
Graph43-17	SEQ ID NO:146	CWWPDGWYC
Graph43-03	SEQ ID NO:147	CKLQLTNQC

Round 4 – 1st try		
Graph42-01	SEQ ID NO:129	CHHNLSSAC
Graph42-02	SEQ ID NO:130	CITGPTGAC
Graph42-03	SEQ ID NO:115	CWWSWHPWC
Graph42-04	SEQ ID NO:131	CPPGPTASC
Graph42-05	SEQ ID NO:132	CHQAGGHQC
Graph42-06	SEQ ID NO:115	CWWSWHPWC
Graph42-07	SEQ ID NO:115	CWWSWHPWC
Graph42-08	SEQ ID NO:115	CWWSWHPWC
Graph42-09	SEQ ID NO:115	CWWSWHPWC
Graph42-10	SEQ ID NO:115	CWWSWHPWC

FIG. 13

Round 5 – 1st try		
Graph5-01	SEQ ID NO:115	CWWSWHPWC
Graph5-04	SEQ ID NO:115	CWWSWHPWC
Graph5-05	SEQ ID NO:115	CWWSWHPWC
Graph5-06	SEQ ID NO:115	CWWSWHPWC
Graph5-07	SEQ ID NO:115	CWWSWHPWC
Graph5-08	SEQ ID NO:115	CWWSWHPWC
Graph5-09	SEQ ID NO:115	CWWSWHPWC
Graph5-10	SEQ ID NO:115	CWWSWHPWC
Graph5-11	SEQ ID NO:115	CWWSWHPWC
Graph5-13	SEQ ID NO:115	CWWSWHPWC
Graph5-14	SEQ ID NO:115	CWWSWHPWC
Graph5-15	SEQ ID NO:115	CWWSWHPWC
Graph5-16	SEQ ID NO:115	CWWSWHPWC
Graph5-17	SEQ ID NO:115	CWWSWHPWC
Graph5-18	SEQ ID NO:115	CWWSWHPWC
Graph5-19	SEQ ID NO:115	CWWSWHPWC
Graph5-12	SEQ ID NO:148	CWHGLGGNC
Graph5-02	SEQ ID NO:149	CHITLLKRC
Graph5-20	SEQ ID NO:150	CESMARPHC

Round 5 – 2nd try		
Graph53-01	SEQ ID NO:151	CHWSWWHPC
Graph53-04	SEQ ID NO:151	CHWSWWHPC
Graph53-06	SEQ ID NO:151	CHWSWWHPC
Graph53-07	SEQ ID NO:151	CHWSWWHPC
Graph53-08	SEQ ID NO:151	CHWSWWHPC
Graph53-11	SEQ ID NO:151	CHWSWWHPC
Graph53-13	SEQ ID NO:151	CHWSWWHPC
Graph53-15	SEQ ID NO:151	CHWSWWHPC
Graph53-16	SEQ ID NO:151	CHWSWWHPC
Graph53-17	SEQ ID NO:151	CHWSWWHPC
Graph53-18	SEQ ID NO:151	CHWSWWHPC
Graph53-19	SEQ ID NO:151	CHWSWWHPC
Graph53-20	SEQ ID NO:151	CHWSWWHPC
Graph53-05	SEQ ID NO:133	CYFSWWHPC
Graph53-10	SEQ ID NO:133	CYFSWWHPC
Graph53-12	SEQ ID NO:133	CYFSWWHPC
Graph53-03	SEQ ID NO:152	CTLLLSRNC
Graph53-14	SEQ ID NO:153	CSSVSYMAC
Graph53-02	SEQ ID NO:154	CHWRWLPAC

FIG. 13

Round 4 – 1st try		
Graph12R4-01	SEQ ID NO:155	WSPGQQRLHNSX
Graph12R4-02	SEQ ID NO:156	DSSNPIFWRPSS
Graph12R4-05	SEQ ID NO:157	EPFPASSLMTIR
Graph12R4-13	SEQ ID NO:158	SYHWDKTPQVLI
Graph12R4-07	SEQ ID NO:159	SGHQLLLNKMPN
Graph12R4-09	SEQ ID NO:160	SIPSEASLSSPR
Graph12R4-12	SEQ ID NO:161	TVPPQLNAQFRS
Graph12R4-14	SEQ ID NO:162	SDNVHTWQAMFK
Graph12R4-06	SEQ ID NO:163	YPSLLKMQPQFS
Graph12R4-15	SEQ ID NO:164	LPIPAHVAPHGP
Graph12R4-16	SEQ ID NO:165	LWGRPFPDLLHQ
Graph12R4-17	SEQ ID NO:166	QTPPWILSHPPQ
Graph12R4-08	SEQ ID NO:167	NHPHPTPARGII
Graph12R4-18	SEQ ID NO:168	HPSSAPWGVALA
Graph12R4-04	SEQ ID NO:169	HWXNHRYSMWGA

Round 5 – 1st try		
Graph12R5-01	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-04	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-07	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-09	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-10	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-12	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-13	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-14	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-15	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-17	SEQ ID NO:170	NHRIWESFWPSA
Graph12R5-03	SEQ ID NO:171	HSSWWLALAKPT
Graph12R5-05	SEQ ID NO:172	SNNDLSPLQTSH
Graph12R5-11	SEQ ID NO:173	SGLPHLSLNAPR
Graph12R5-02	SEQ ID NO:174	SWPLYSRDSGLG
Graph12R5-06	SEQ ID NO:175	LPGWPLAERVGQ

Round 5 – 2nd try		
Graph12R52-01	SEQ ID NO:176	SHPWNAQRELSV
Graph12R52-14	SEQ ID NO:176	SHPWNAQRELSV
Graph12R52-16	SEQ ID NO:176	SHPWNAQRELSV
Graph12R52-17	SEQ ID NO:176	SHPWNAQRELSV
Graph12R52-05	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R52-06	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R52-08	SEQ ID NO:178	YWPSKHWWWLAP
Graph12R52-10	SEQ ID NO:178	YWPSKHWWWLAP
Graph12R52-15	SEQ ID NO:178	YWPSKHWWWLAP
Graph12R52-02	SEQ ID NO:179	SSAWWSYWPPVA
Graph12R52-03	SEQ ID NO:180	APLGFNSMRLPA
Graph12R52-18	SEQ ID NO:181	WNMRWLPTWAPA
Graph12R52-07	SEQ ID NO:182	WPRYPSTLVSSH
Graph12R52-09	SEQ ID NO:183	GKESVPPPRIYA
Graph12R52-12	SEQ ID NO:184	LTLDMKRTSGPL
Graph12R52-13	SEQ ID NO:185	LSTHTTESRSMV
Graph12R52-11	SEQ ID NO:186	EYLSAIVAGPWP

FIG. 14

Round 6 – 2nd try		
Graph12R62-01	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R62-05	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R62-06	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R62-09	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R62-12	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R62-16	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R62-18	SEQ ID NO:177	VSRHQSWHPHDL
Graph12R62-02	SEQ ID NO:178	YWPSKHWWWLA
Graph12R62-04	SEQ ID NO:178	YWPSKHWWWLAP
Graph12R62-07	SEQ ID NO:178	YWPSKHWWWLAP
Graph12R62-14	SEQ ID NO:178	YWPSKHWWWLAP
Graph12R62-03	SEQ ID NO:187	QFKWWHSLSPTP
Graph12R62-11	SEQ ID NO:187	QFKWWHSLSPTP
Graph12R62-17	SEQ ID NO:179	SSAWWSYWPPVA
Graph12R62-08	SEQ ID NO:181	WNMRWLPTWAPA
Graph12R62-15	SEQ ID NO:176	SHPWNAQRELSV

FIG. 14

Round 4 – 1st try		
Hipco12R4-01	SEQ ID NO:176	SHPWNAQRELSV
Hipco12R4-02	SEQ ID NO:176	SHPWNAQRELSV
Hipco12R4-03	SEQ ID NO:176	SHPWNAQRELSV
Hipco12R4-05	SEQ ID NO:176	SHPWNAQRELSV
Hipco12R4-06	SEQ ID NO:176	SHPWNAQRELSV
Hipco12R4-08	SEQ ID NO:176	SHPWNAQRELSV
Hipco12R4-10	SEQ ID NO:176	SHPWNAQRELSV
Hipco12R4-04	SEQ ID NO:188	APTPLIGKRLVQ
Hipco12R4-07	SEQ ID NO:189	LINPRDHVLAPQ

Round 3 – 3rd try		
Hipco12R34-01	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R34-05	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R34-12	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R34-14	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R34-15	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R34-03	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R34-18	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R34-02	SEQ ID NO:195	STPALMTLIART
Hipco12R34-06	SEQ ID NO:196	TSNFINRMNPGL
Hipco12R34-08	SEQ ID NO:197	TSASTRPELHYP
Hipco12R34-07	SEQ ID NO:198	NLLEVISLPHRG
Hipco12R34-04	SEQ ID NO:199	QHPNNAHVRQFP
Hipco12R34-11	SEQ ID NO:200	QHANNQAWNNLR
Hipco12R34-13	SEQ ID NO:201	QHYPGRAIPHST
Hipco12R34-09	SEQ ID NO:202	VPPPHPQFDHLI
Hipco12R34-10	SEQ ID NO:203	LKMNPSISSSLK
Hipco12R34-17	SEQ ID NO:204	HWDPFSLSAYFP

FIG. 15

Round 3 – 2nd try		
Hipco12R33-01	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-03	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-05	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-06	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-07	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-08	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-09	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-10	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-12	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-14	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-15	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-16	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-17	SEQ ID NO:190	LLADTTHHRPWT
Hipco12R33-02	SEQ ID NO:191	QASISPLWTPTP
Hipco12R33-13	SEQ ID NO:192	NSXLHLAHQPHK

Round 4 – 3rd try		
Hipco12R44-01	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-02	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-05	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-06	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-07	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-12	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-15	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-16	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-17	SEQ ID NO:194	DMPRTTMSPPPR
Hipco12R44-03	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R44-08	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R44-10	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R44-13	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R44-14	SEQ ID NO:193	TKNMLSLPVGPG
Hipco12R44-18	SEQ ID NO:205	WSPGQQRLHNST

FIG. 15

Round 4 – 1st try		
HOPG12R4-03	SEQ ID NO:206	NMTKHPLAYTEP
HOPG12R4-05	SEQ ID NO:206	NMTKHPLAYTEP
HOPG12R4-08	SEQ ID NO:170	NHRIWESFWPSA
HOPG12R4-02	SEQ ID NO:207	HMPTKSASQTYF
HOPG12R4-04	SEQ ID NO:171	HSSWWLALAKPT
HOPG12R4-07	SEQ ID NO:208	HNAYWHWPPSMT
HOPG12R4-06	SEQ ID NO:209	VLPPKPMRQPVA
HOPG12R4-01	SEQ ID NO:210	SLHKISQLSFAS

Round 5 – 1st try		
HOPG12R5-04	SEQ ID NO:211	WHSRLPPMTVAF
HOPG12R5-06	SEQ ID NO:211	WHSRLPPMTVAF
HOPG12R5-07	SEQ ID NO:211	WHSRLPPMTVAF
HOPG12R5-17	SEQ ID NO:211	WHSRLPPMTVAF
HOPG12R5-09	SEQ ID NO:163	YPSLLKMQPQFS
HOPG12R5-03	SEQ ID NO:163	YPSLLKMQPQFS
HOPG12R5-12	SEQ ID NO:212	TPWFQWHQWNLN
HOPG12R5-10	SEQ ID NO:56	SVSVGMKPSPRP
HOPG12R5-01	SEQ ID NO:213	SDTISRLHVSMT
HOPG12R5-13	SEQ ID NO:167	NHPHPTPARGII
HOPG12R5-18	SEQ ID NO:214	NPYHPTIPQSVH
HOPG12R5-08	SEQ ID NO:215	LPSAKLPPGPPK

Round 5 – 2nd try		
HOPG12R52-02	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R52-08	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R52-11	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R52-12	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R52-14	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R52-18	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R52-01	SEQ ID NO:217	SNFTTQMTFYTG
HOPG12R52-05	SEQ ID NO:217	SNFTTQMTFYTG
HOPG12R52-06	SEQ ID NO:217	SNFTTQMTFYTG
HOPG12R52-10	SEQ ID NO:218	KMDRHDPSPALL
HOPG12R52-15	SEQ ID NO:218	KMDRHDPSPALL
HOPG12R52-17	SEQ ID NO:218	KMDRHDPSPALL
HOPG12R52-13	SEQ ID NO:219	MPAVMSSAQVPR
HOPG12R52-16	SEQ ID NO:219	MPAVMSSAQVPR
HOPG12R52-07	SEQ ID NO:220	DRAPLIPFASQH
HOPG12R52-03	SEQ ID NO:221	DQYIQQAHRSHI
HOPG12R52-09	SEQ ID NO:222	HARINPSFPLPI
HOPG12R52-04	SEQ ID NO:223	GWWPYAALRALS

FIG. 16

Round 6 – 1st try		
HOPG12R6-01	SEQ ID NO:190	LLADTTHHRPWT
HOPG12R6-05	SEQ ID NO:190	LLADTTHHRPWT
HOPG12R6-06	SEQ ID NO:224	TAATSSPHSRSP
HOPG12R6-10	SEQ ID NO:213	SDTISRLHVSMT
HOPG12R6-16	SEQ ID NO:225	STTGQSPALAPP
HOPG12R6-13	SEQ ID NO:226	HSSWYIQHFPPL
HOPG12R6-17	SEQ ID NO:211	WHSRLPPMTVAF
HOPG12R6-12	SEQ ID NO:227	GSHSNPTPLTPR

Round 6 – 2nd try		
HOPG12R62-03	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-06	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-09	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-11	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-12	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-13	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-14	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-17	SEQ ID NO:216	TSNPHTRHYYPI
HOPG12R62-02	SEQ ID NO:218	KMDRHDPSPALL
HOPG12R62-04	SEQ ID NO:218	KMDRHDPSPALL
HOPG12R62-15	SEQ ID NO:218	KMDRHDPSPALL
HOPG12R62-07	SEQ ID NO:217	SNFTTQMTFYTG
HOPG12R62-16	SEQ ID NO:217	SNFTTQMTFYTG
HOPG12R62-10	SEQ ID NO:219	MPAVMSSAQVPR
HOPG12R62-18	SEQ ID NO:219	MPAVMSSAQVPR
HOPG12R62-05	SEQ ID NO:222	HARINPSFPLPI
HOPG12R62-01	SEQ ID NO:220	DRAPLIPFASQH
HOPG12R62-08	SEQ ID NO:228	YTGVLDTKATQN

FIG. 16

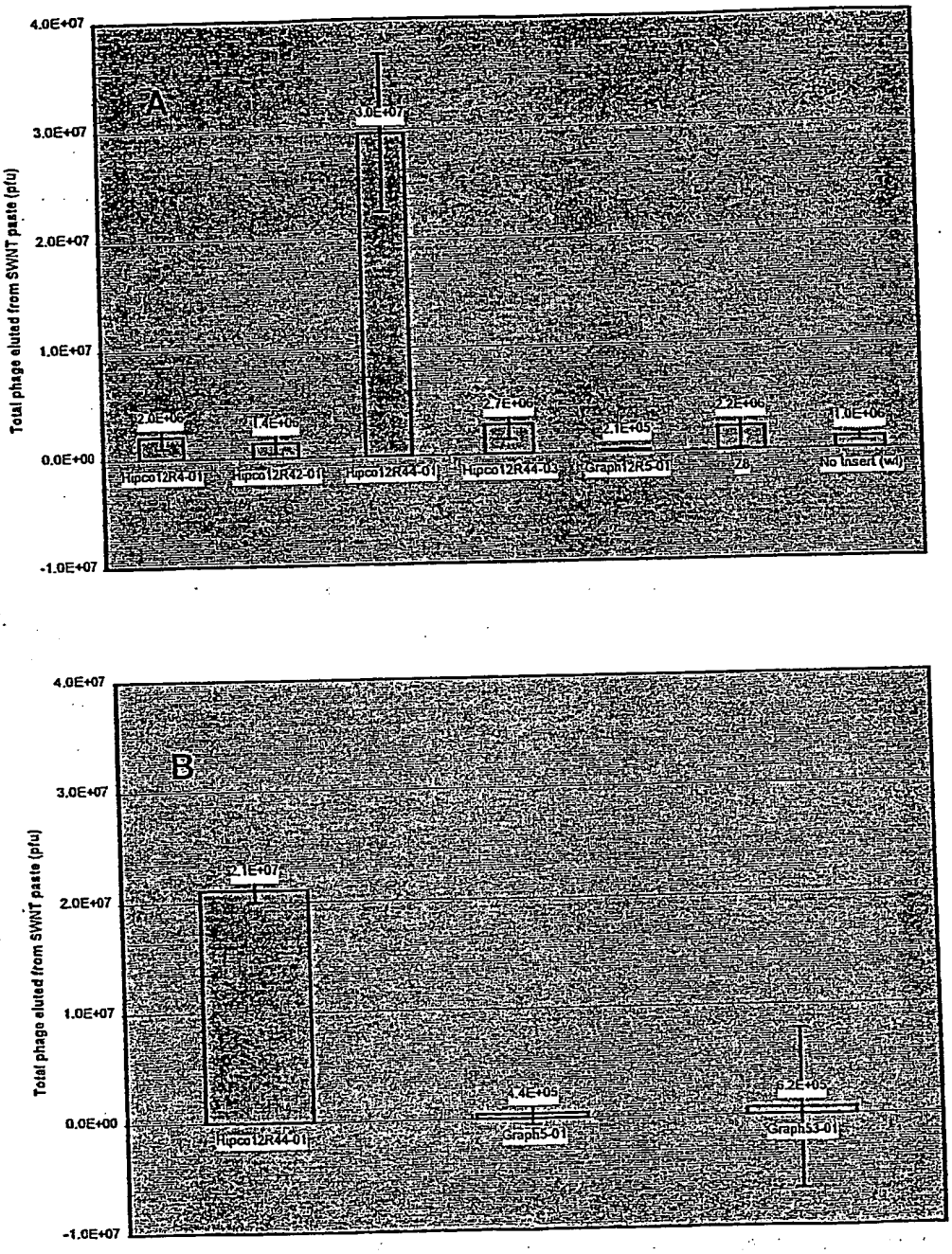

A
Total phage eluted from SWNT paste (pfu)
4.0E+07
3.0E+07
2.0E+07
1.0E+07
0.0E+00
-1.0E+07
2.0E+06
1.4E+06
3.0E+07
2.7E+06
2.1E+05
2.2E+06
1.0E+06
Hipco12R4-01
Hipco12R42-01
Hipco12R44-01
Hipco12R44-03
Graph12R5-01
Z8
No Insert (wt)
B
Total phage eluted from SWNT paste (pfu)
4.0E+07
3.0E+07
2.0E+07
1.0E+07
0.0E+00
-1.0E+07
2.1E+07
4.4E+05
6.2E+05
Hipco12R44-01
Graph5-01
Graph53-01

Fig. 17

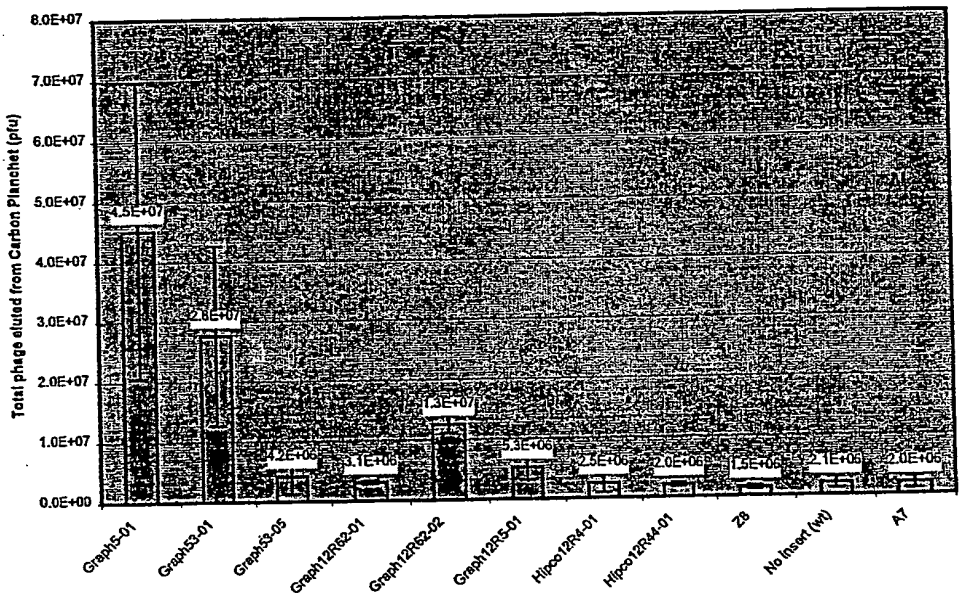

Total phage eluted from Carbon Planchet (pfu)
8.0E+07
7.0E+07
6.0E+07
5.0E+07
4.0E+07
3.0E+07
2.0E+07
1.0E+07
0.0E+00
4.5E+07
2.8E+07
4.2E+06
3.1E+06
1.3E+07
5.3E+06
2.5E+06
2.0E+06
1.5E+06
2.1E+06
2.0E+06
Graph5-01
Graph53-01
Graph53-05
Graph12R62-01
Graph12R62-02
Graph12R5-01
Hipco12R4-01
Hipco12R44-01
Z8
No Insert (wt)
A7

Fig. 18

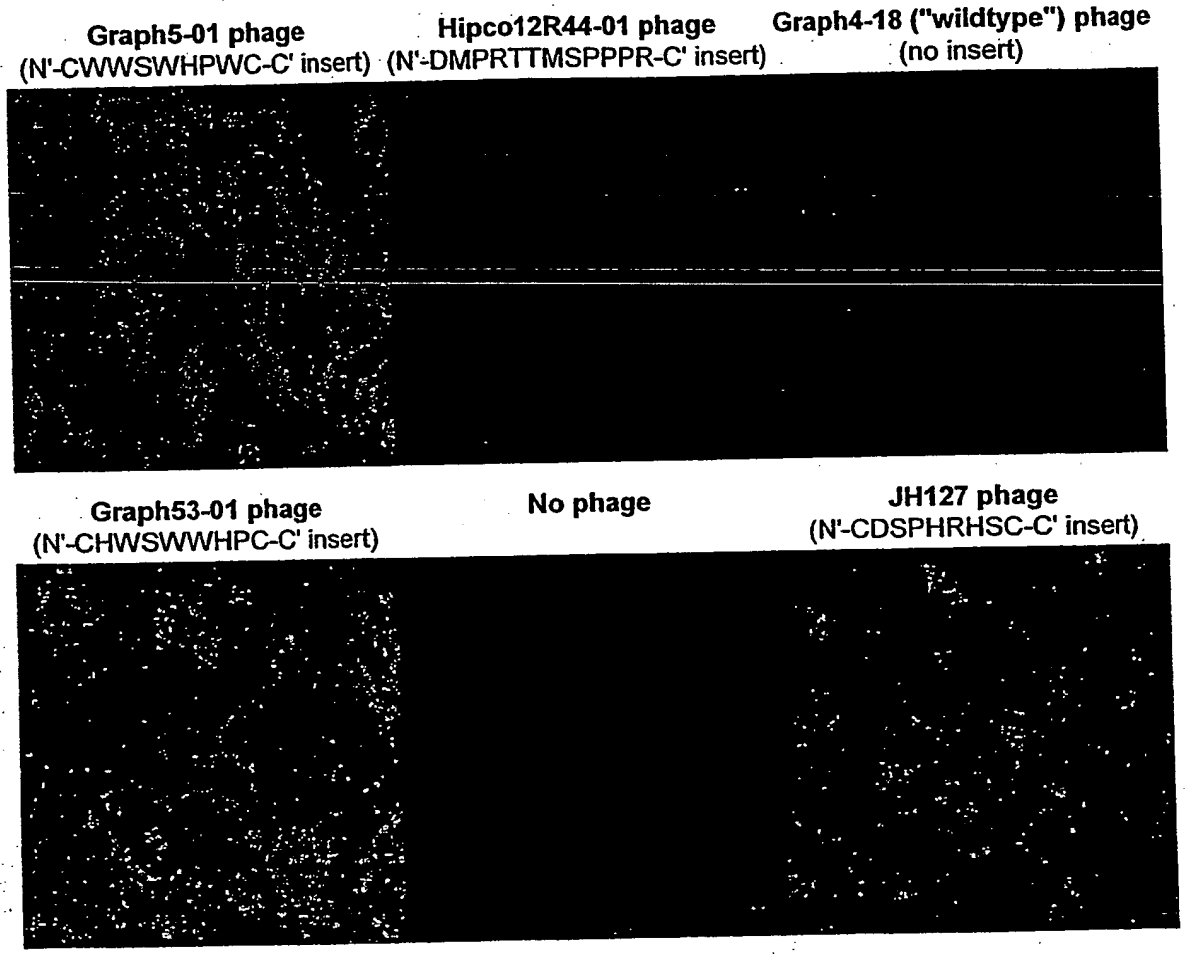

Graph5-01 phage
(N'-CWWSWHPWC-C' insert)
Hipco12R44-01 phage
(N'-DMPRTTMSPPPR-C' insert)
Graph4-18 ("wildtype") phage
(no insert)
Graph53-01 phage
(N'-CHWSWWHPC-C' insert)
No phage
JH127 phage
(N'-CDSPHRHSC-C' insert)

Fig. 19

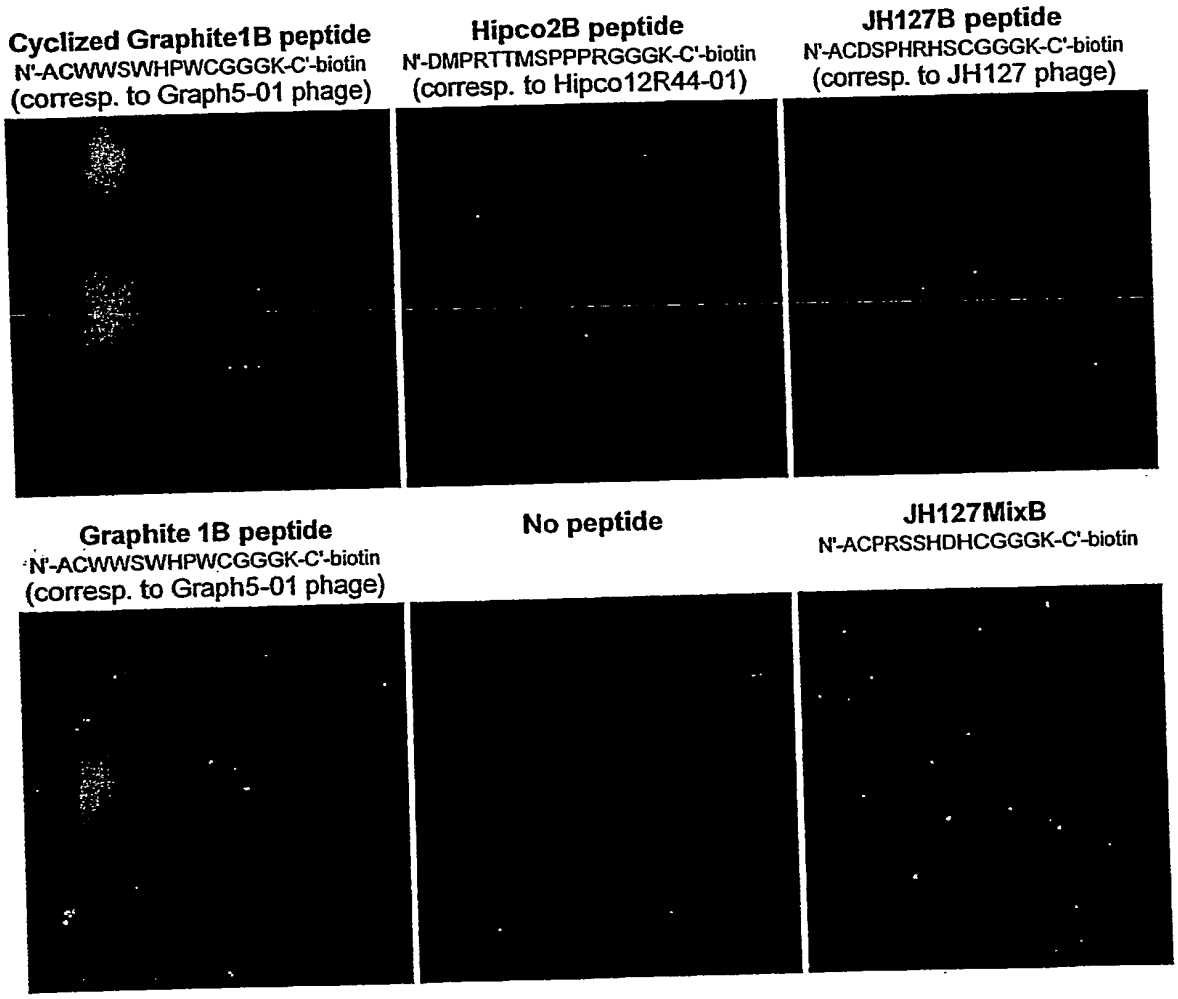

Cyclized Graphite1B peptide
N'-ACWWSWHPWCGGGK-C'-biotin
(corresp. to Graph5-01 phage)
Hipco2B peptide
N'-DMPRTTMSPPPRGGGK-C'-biotin
(corresp. to Hipco12R44-01)
JH127B peptide
N'-ACDSPHRHSCGGGK-C'-biotin
(corresp. to JH127 phage)
Graphite 1B peptide
N'-ACWWSWHPWCGGGK-C'-biotin
(corresp. to Graph5-01 phage)
No peptide
JH127MixB
N'-ACPRSSHDHCGGGK-C'-biotin

Fig. 20

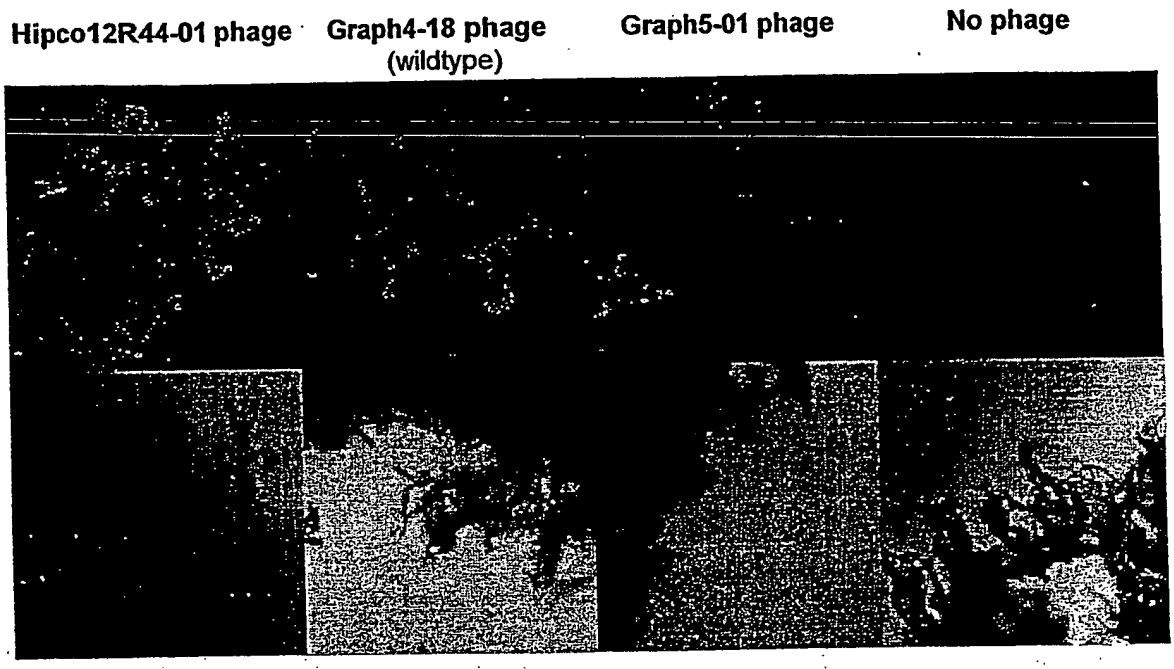
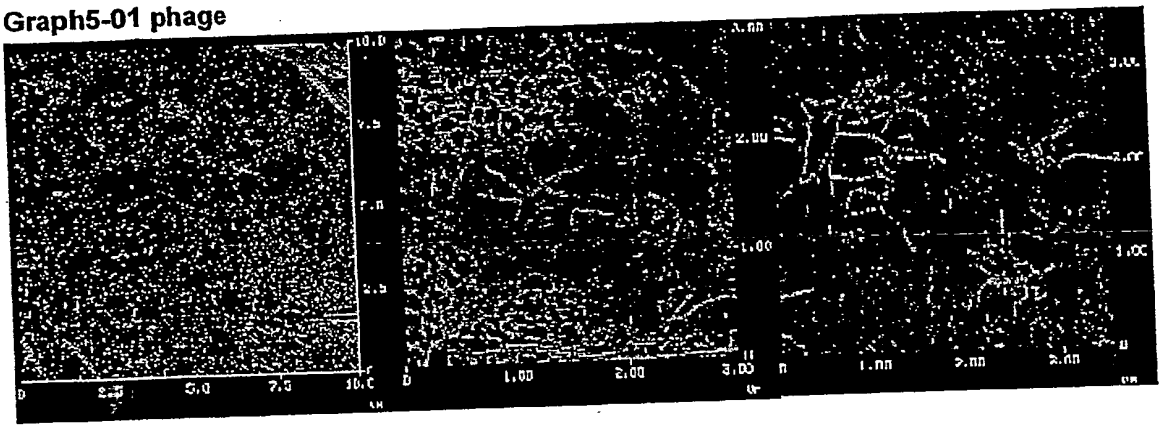

Hipco12R44-01 phage
Graph4-18 phage
(wildtype)
Graph5-01 phage
No phage

Fig. 21

Graph5-01 phage



Graph4-18 (wildtype) phage

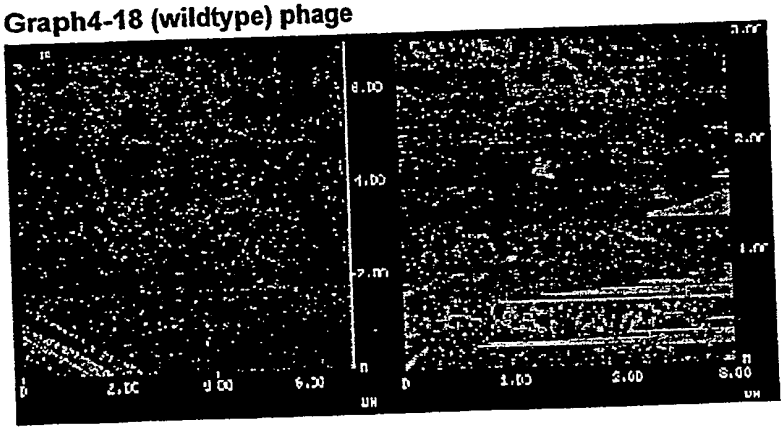


Fig. 22

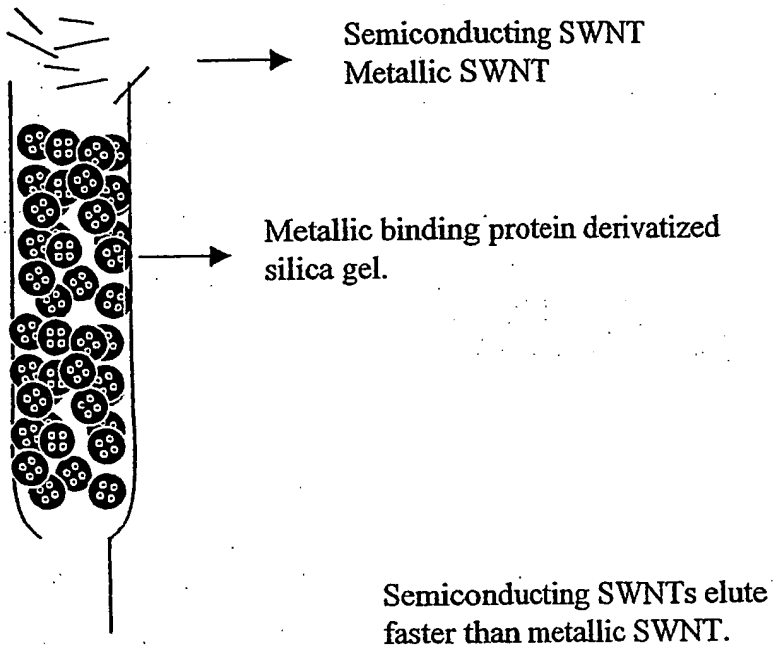

Semiconducting SWNT
Metallic SWNT
Metallic binding protein derivatized silica gel.
Semiconducting SWNTs elute faster than metallic SWNT.

Fig. 23.

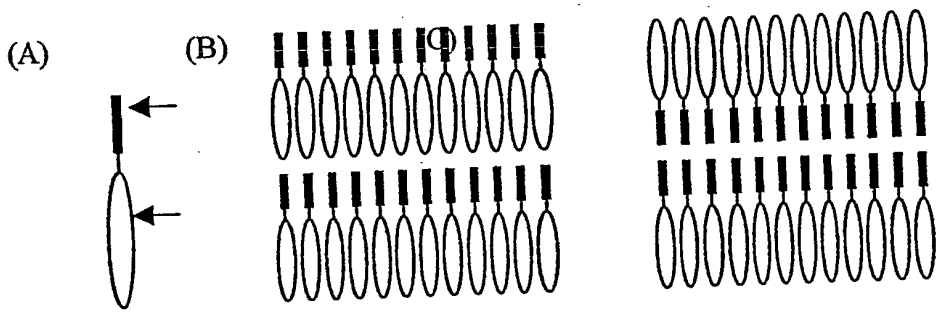


Fig. 24

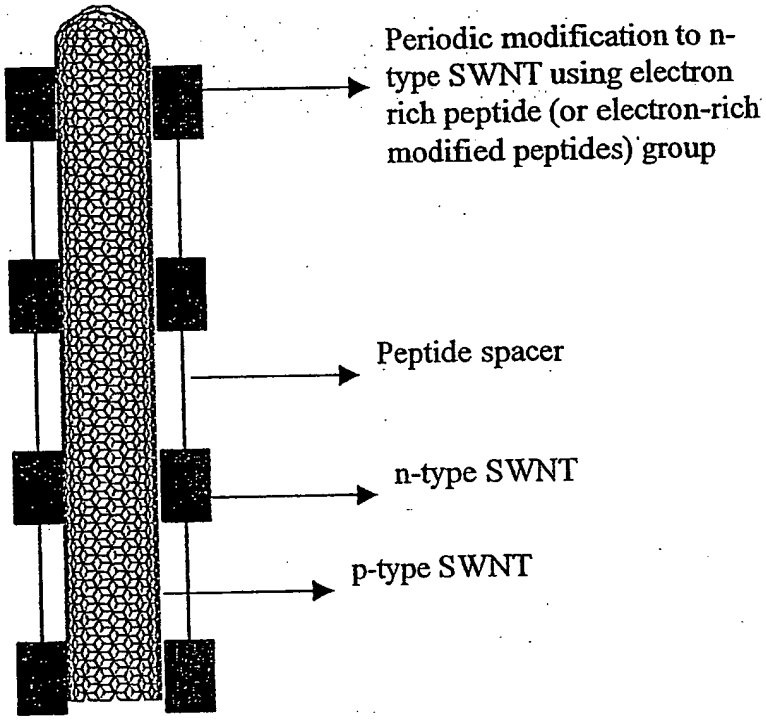

Periodic modification to n-type SWNT using electron rich peptide (or electron-rich modified peptides) group
Peptide spacer
n-type SWNT
p-type SWNT

Fig. 25

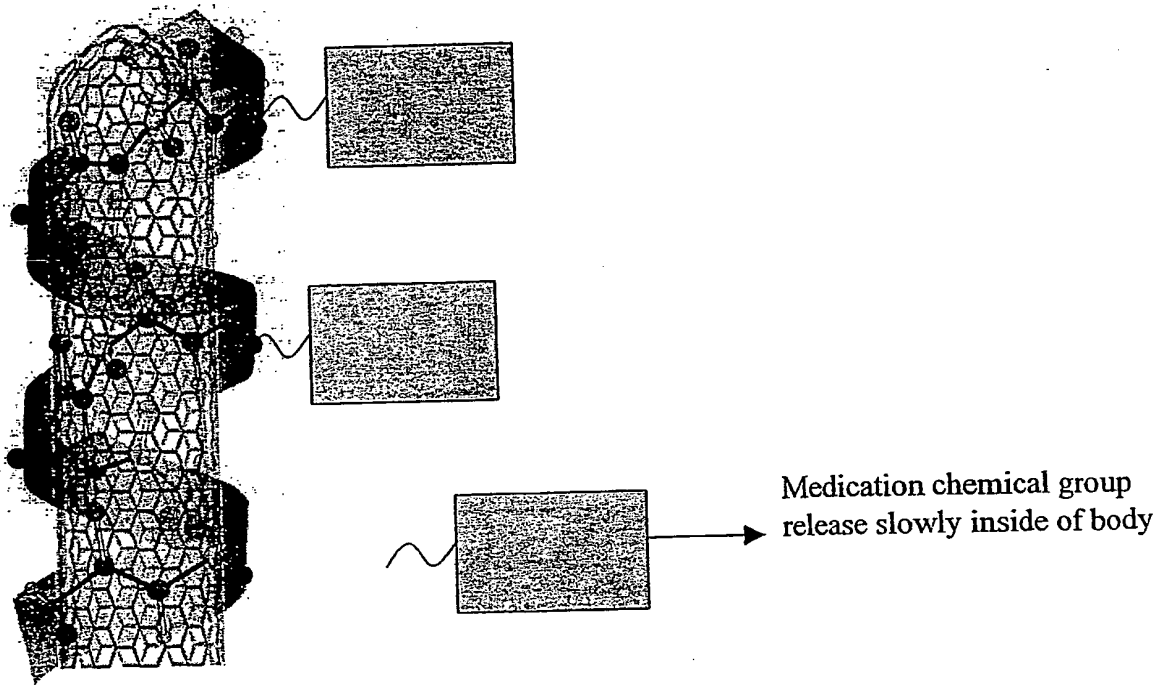


Fig. 26

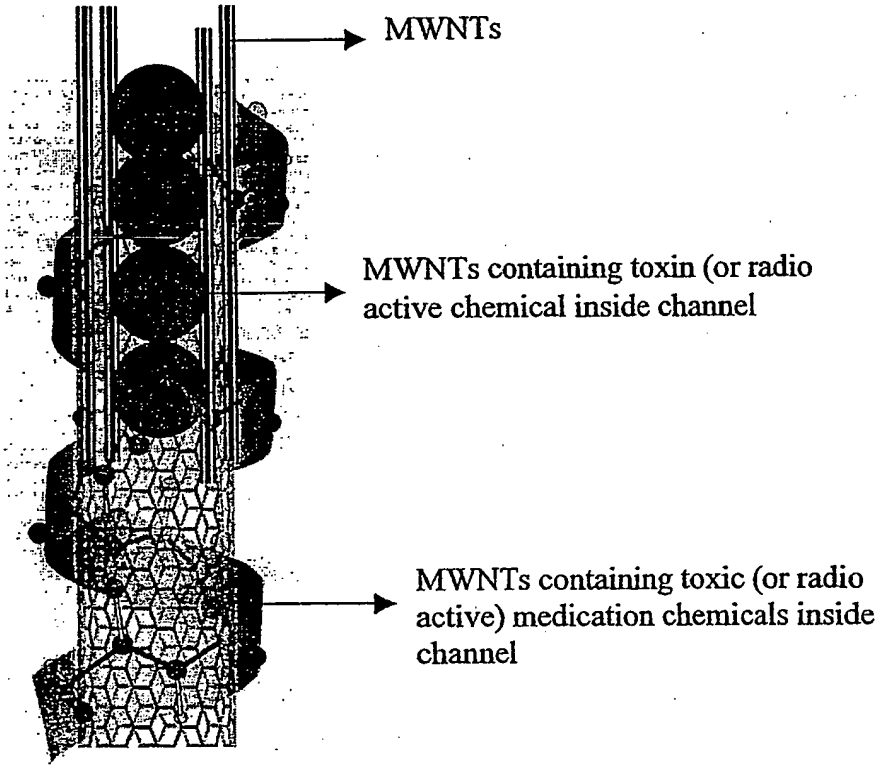

MWNTs
MWNTs containing toxin (or radio active chemical inside channel
MWNTs containing toxic (or radio active) medication chemicals inside channel

Fig. 27

SEQUENCE LISTING

<110> Belcher, Angela M
Smalley, Richard E.
Ryan, Esther
Lee, Seung-Wuk

<120> BIOLOGICAL CONTROL OF NANOPARTICLES

<130> 119927-1066

<140> N/A
<141> 2002-09-25

<150> 60/325,664
<151> 2001-09-28

<160> 245

<170> PatentIn version 3.1

<210> 1
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> artifical peptide

<400> 1

Ala Met Ala Gly Thr Thr Ser Asp Pro Ser Thr Val
1 5 10

<210> 2
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 2

Ala Ala Ser Pro Thr Gln Ser Met Ser Gln Ala Pro
1 5 10

<210> 3
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 3

His Thr His Thr Asn Asn Asp Ser Pro Asn Gln Ala
1 5 10

<210> 4
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 4

Asp Thr Gln Gly Phe His Ser Arg Ser Ser Ser Ala
1 5 10

<210> 5
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 5

Thr Ser Ser Ser Ala Leu Gln Pro Ala His Ala Trp
1 5 10

<210> 6
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 6

Ser Glu Ser Ser Pro Ile Ser Leu Asp Tyr Arg Ala
1 5 10

<210> 7
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 7

Ser Thr His Asn Tyr Gln Ile Pro Arg Pro Pro Thr
1 5 10

<210> 8
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 8

His Pro Phe Ser Asn Glu Pro Leu Gln Leu Ser Ser
1 5 10

<210> 9
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 9

Gly Thr Leu Ala Asn Gln Gln Ile Phe Leu Ser Ser
1 5 10

<210> 10
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 10

His Gly Asn Pro Leu Pro Met Thr Pro Phe Pro Gly
1 5 10

<210> 11
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 11

Arg Leu Glu Leu Ala Ile Pro Leu Gln Gly Ser Gly
1 5 10

<210> 12
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 12

Cys His Ala Ser Asn Arg Leu Ser Cys
1 5

<210> 13
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 13

Ser Met Asp Arg Ser Asp Met Thr Met Arg Leu Pro
1 5 10

<210> 14
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 14

Gly Thr Phe Thr Pro Arg Pro Thr Pro Ile Tyr Pro
1 5 10

<210> 15
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 15

Gln Met Ser Glu Asn Leu Thr Ser Gln Ile Glu Ser

1 5 10

<210> 16
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 16

Asp Met Leu Ala Arg Leu Arg Ala Thr Ala Gly Pro
1 5 10

<210> 17
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 17

Ser Gln Thr Trp Leu Leu Met Ser Pro Val Ala Thr
1 5 10

<210> 18
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 18

Ala Ser Pro Asp Gln Gln Val Gly Pro Leu Tyr Val
1 5 10

<210> 19
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 19

Leu Thr Trp Ser Pro Leu Gln Thr Val Ala Arg Phe
1 5 10

<210> 20
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 20

Gln Ile Ser Ala His Gln Met Pro Ser Arg Pro Ile
1 5 10

<210> 21
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 21

Ser Met Lys Tyr Asn Leu Ile Val Asp Ser Pro Tyr
1 5 10

<210> 22
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 22

Gln Met Pro Ile Arg Asn Gln Leu Ala Trp Pro Met
1 5 10

<210> 23
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 23

Thr Gln Asn Leu Glu Ile Arg Glu Pro Leu Thr Pro
1 5 10

<210> 24
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 24

Tyr Pro Met Ser Pro Ser Pro Tyr Pro Tyr Gln Leu
1 5 10

<210> 25
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 25

Ser Phe Met Ile Gln Pro Thr Pro Leu Pro Pro Ser
1 5 10

<210> 26
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 26

Gly Leu Ala Pro His Ile His Ser Leu Asn Glu Ala
1 5 10

<210> 27
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 27

Met Gln Phe Pro Val Thr Pro Tyr Leu Asn Ala Ser
1 5 10

<210> 28
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 28

Ser Pro Gly Asp Ser Leu Lys Lys Leu Ala Ala Ser
1 5 10

<210> 29
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 29

Gly Tyr His Met Gln Thr Leu Pro Gly Pro Val Ala
1 5 10

<210> 30
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 30

Ser Leu Thr Pro Leu Thr Thr Ser His Leu Arg Ser
1 5 10

<210> 31
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 31

Thr Leu Thr Asn Gly Pro Leu Arg Pro Phe Thr Gly
1 5 10

<210> 32

<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 32

Leu Asn Thr Pro Lys Pro Phe Thr Leu Gly Gln Asn
1 5 10

<210> 33
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 33

Cys Asp Leu Gln Asn Tyr Lys Ala Cys
1 5

<210> 34
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 34

Cys Arg His Pro His Thr Arg Leu Cys
1 5

<210> 35
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 35

Cys Ala Asn Leu Lys Pro Lys Ala Cys
1 5

<210> 36
<211> 9

<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 36

Cys Tyr Ile Asn Pro Pro Lys Val Cys
1 5

<210> 37
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 37

Cys Asn Asn Lys Val Pro Val Leu Cys
1 5

<210> 38
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 38

Cys His Ala Ser Lys Thr Pro Leu Cys
1 5

<210> 39
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 39

Cys Ala Ser Gln Leu Tyr Pro Ala Cys
1 5

<210> 40
<211> 9
<212> PRT

<213> artificial sequence

<220>
<223> peptide

<400> 40

Cys Asn Met Thr Gln Tyr Pro Ala Cys
1 5

<210> 41
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 41

Cys Phe Ala Pro Ser Gly Pro Ala Cys
1 5

<210> 42
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 42

Cys Pro Val Trp Ile Gln Ala Pro Cys
1 5

<210> 43
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 43

Cys Gln Val Ala Val Asn Pro Leu Cys
1 5

<210> 44
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 44

Cys Gln Pro Glu Ala Met Pro Ala Cys
1 5

<210> 45
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 45

Cys His Pro Thr Met Pro Leu Ala Cys
1 5

<210> 46
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 46

Cys Pro Pro Phe Ala Ala Pro Ile Cys
1 5

<210> 47
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 47

Cys Asn Lys His Gln Pro Met His Cys
1 5

<210> 48
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 48

Cys Phe Pro Met Arg Ser Asn Gln Cys
1 5

<210> 49
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 49

Cys Gln Ser Met Pro His Asn Arg Cys
1 5

<210> 50
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 50

Cys Asn Asn Pro Met His Gln Asn Cys
1 5

<210> 51
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 51

Cys His Met Ala Pro Arg Trp Gln Cys
1 5

<210> 52
<211> 9
<212> PRT
<213> artificial sequence

<220>

<223> peptide

<400> 52

His Val His Ile His Ser Arg Pro Met
1 5

<210> 53
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 53

Leu Pro Asn Met His Pro Leu Pro Leu
1 5

<210> 54
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 54

Leu Pro Leu Arg Leu Pro Pro Met Pro
1 5

<210> 55
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 55

His Ser Met Ile Gly Thr Pro Thr Thr
1 5

<210> 56
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 56

Ser Val Ser Val Gly Met Lys Pro Ser
1 5

<210> 57
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 57

Leu Asp Ala Ser Phe Met Gln Asp Trp
1 5

<210> 58
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 58

Thr Pro Pro Ser Tyr Gln Met Ala Met
1 5

<210> 59
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 59

Tyr Pro Gln Leu Val Ser Met Ser Thr
1 5

<210> 60
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 60

Gly Tyr Ser Thr Ile Asn Met Tyr Ser
1 5

<210> 61
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 61

Asp Arg Met Leu Leu Pro Phe Asn Leu
1 5

<210> 62
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 62

Ile Pro Met Thr Pro Ser Tyr Asp Ser
1 5

<210> 63
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 63

Met Tyr Ser Pro Arg Pro Pro Ala Leu
1 5

<210> 64
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 64

Gln Pro Thr Thr Asp Leu Met Ala His
1 5

<210> 65
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 65

Ala Thr His Val Gln Met Ala Trp Ala
1 5

<210> 66
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 66

Ser Met His Ala Thr Leu Thr Pro Met
1 5

<210> 67
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 67

Ser Gly Pro Ala His Gly Met Phe Ala
1 5

<210> 68
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 68

Ile Ala Asn Arg Pro Tyr Ser Ala Gln
1 5

<210> 69
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 69

Val Met Thr Gln Pro Thr Arg
1 5

<210> 70
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 70

His Met Arg Pro Leu Ser Ile
1 5

<210> 71
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 71

Leu Thr Arg Ser Pro Leu His Val Asp Gln Arg Arg
1 5 10

<210> 72
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 72

Val Ile Ser Asn His Ala Glu Ser Ser Arg Arg Leu

1 5 10

<210> 73
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 73

His Thr His Ile Pro Asn Gln
1 5

<210> 74
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 74

Leu Ala Pro Val Ser Pro Pro
1 5

<210> 75
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 75

Cys Met Thr Ala Gly Lys Asn Thr Cys
1 5

<210> 76
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 76

Cys Gln Thr Leu Trp Arg Asn Ser Cys
1 5

<210> 77
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 77

Cys Thr Ser Val His Thr Asn Thr Cys
1 5

<210> 78
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 78

Cys Pro Ser Leu Ala Met Asn Ser Cys
1 5

<210> 79
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 79

Cys Ser Asn Asn Thr Val His Ala Cys
1 5

<210> 80
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 80

Cys Leu Pro Ala Gln Gly His Val Cys
1 5

<210> 81
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 81

Cys Leu Pro Ala Gln Val His Val Cys
1 5

<210> 82
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 82

Cys Pro Pro Lys Asn Val Arg Leu Cys
1 5

<210> 83
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 83

Cys Pro His Ile Asn Ala His Ala Cys
1 5

<210> 84
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 84

Cys Ile Val Asn Leu Ala Arg Ala Cys
1 5

<210> 85
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 85

Thr Met Gly Phe Thr Ala Pro Arg Phe Pro His Tyr
1 5 10

<210> 86
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 86

Ala Thr Gln Ser Tyr Val Arg His Pro Ser Leu Gly
1 5 10

<210> 87
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 87

Thr Ser Thr Thr Gln Gly Ala Leu Ala Tyr Leu Phe
1 5 10

<210> 88
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 88

Asp Pro Pro Trp Ser Ala Ile Val Arg His Arg Asp
1 5 10

<210> 89

<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 89

Phe Asp Asn Lys Pro Phe Leu Arg Val Ala Ser Glu
1 5 10

<210> 90
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 90

His Gln Ser His Thr Gln Gln Asn Lys Arg His Leu
1 5 10

<210> 91
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 91

Thr Ser Thr Thr Gln Gly Ala Leu Ala Tyr Leu Phe
1 5 10

<210> 92
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 92

Lys Thr Pro Ile His Thr Ser Ala Trp Glu Phe Gln
1 5 10

<210> 93
<211> 12

<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 93

Asp Leu Phe His Leu Lys Pro Val Ser Asn Glu Lys
1 5 10

<210> 94
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 94

Lys Pro Phe Trp Thr Ser Ser Pro Asp Val Met Thr
1 5 10

<210> 95
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 95

Pro Trp Ala Ala Thr Ser Lys Pro Pro Tyr Ser Ser
1 5 10

<210> 96
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 96

Cys Gln Asn Pro Met Gln Thr Phe Cys
1 5

<210> 97
<211> 9
<212> PRT

<213> artificial sequence

<220>
<223> peptide

<400> 97

Cys Asn Gln Leu Ser Thr Arg Pro Cys
1 5

<210> 98
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 98

Cys Leu Gln Asn Arg Gln Ser Gln Cys
1 5

<210> 99
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 99

Cys Gln Leu Gln Arg Gln Trp Asn Cys
1 5

<210> 100
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 100

Cys Gln Val Asn Ser Ala His Gln Cys
1 5

<210> 101
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 101

Cys Phe Pro Met Arg Ser Asn Gln Cys
1 5

<210> 102
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 102

Cys Pro Pro Gln Pro Asn Arg Gln Cys
1 5

<210> 103
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 103

Cys Gln Met Pro Met Gln His Asn Cys
1 5

<210> 104
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 104

Cys Ala Asn Val Ala Gln Arg Asn Cys
1 5

<210> 105
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 105

Cys Asn Asn Lys Gln Leu Tyr Tyr Cys
1 5

<210> 106
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 106

Cys Gln Thr Ala Trp Ile Gly Gln Cys
1 5

<210> 107
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 107

Cys Gln Ser Ala Asn Lys Leu Thr Cys
1 5

<210> 108
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 108

Cys Ile Pro Tyr Thr Met Ala Met Cys
1 5

<210> 109
<211> 9
<212> PRT
<213> artificial sequence

<220>

<223> peptide

<400> 109

Cys Leu Pro Ser Tyr His Asn Asn Cys
1 5

<210> 110
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 110

Cys Val Ser Val Ala His Lys Asp Cys
1 5

<210> 111
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 111

Cys Glu Val Thr Thr Leu Tyr Arg Cys
1 5

<210> 112
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 112

Cys Glu Leu Thr Ala Phe Pro Ala Cys
1 5

<210> 113
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 113

Cys Thr Leu Ala Ser Pro His Gln Cys
1 5

<210> 114
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 114

Cys Pro Leu Thr Gly Gly Pro Thr Cys
1 5

<210> 115
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 115

Cys Trp Trp Ser Trp His Pro Trp Cys
1 5

<210> 116
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 116

Cys Gln Lys Ser Gly Val His Leu Cys
1 5

<210> 117
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 117

Cys Leu Phe Asn Ala Leu Ile Arg Cys
1 5

<210> 118
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 118

Cys Val Met Trp Thr Ser His Ser Cys
1 5

<210> 119
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 119

Cys Val Ser Arg Trp Arg Ala Ser Cys
1 5

<210> 120
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 120

Cys Ser Ser Trp Glu Pro Lys Ser Cys
1 5

<210> 121
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 121

Cys Thr Leu Thr Gly Pro Phe Ala Cys
1 5

<210> 122
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 122

Cys Pro Pro Val Leu Gly Asn Leu Cys
1 5

<210> 123
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 123

Cys Pro His Ala Pro Ser Gly Pro Cys
1 5

<210> 124
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 124

Cys Pro Leu His Lys Asn Gly Lys Cys
1 5

<210> 125
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 125

Cys Arg Ser His His Ser Trp Ser Cys
1 5

<210> 126
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 126

Cys Lys Gln Phe Leu Ser Leu Ser Cys
1 5

<210> 127
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 127

Cys Asp Asp Ala Ser Leu Arg His Cys
1 5

<210> 128
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 128

Cys Asp Asn Arg Gly Ser Gln Phe Cys
1 5

<210> 129
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 129

Cys His His Asn Leu Ser Ser Ala Cys

1 5

<210> 130
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 130

Cys Ile Thr Gly Pro Thr Gly Ala Cys
1 5

<210> 131
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 131

Cys Pro Pro Gly Pro Thr Ala Ser Cys
1 5

<210> 132
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 132

Cys His Gln Ala Gly Gly His Gln Cys
1 5

<210> 133
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 133

Cys Tyr Phe Ser Trp Trp His Pro Cys
1 5

<210> 134
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 134

Cys Ser Pro Val Lys Tyr Pro Ser Cys
1 5

<210> 135
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 135

Cys Thr Ser His Phe Lys Leu His Cys
1 5

<210> 136
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 136

Cys Gln Gln Gly Thr Ala Pro Leu Cys
1 5

<210> 137
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 137

Cys Gln Glu His Ser Ala Lys Ser Cys
1 5

<210> 138
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 138

Cys Gln Thr Glu Asp Leu Pro Arg Cys
1 5

<210> 139
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 139

Cys Asn Arg Thr Ser Pro Ala His Cys
1 5

<210> 140
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 140

Cys Gln Gly Asn His Ile Gly Leu Cys
1 5

<210> 141
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 141

Cys Leu Asn Asn Tyr Thr His Thr Cys
1 5

<210> 142
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 142

Cys Leu Thr Thr Ala Ser Thr Lys Cys
1 5

<210> 143
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 143

Cys Leu Leu Ser Leu Arg Pro Ala Cys
1 5

<210> 144
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 144

Cys Asp Ser Gln Leu Trp Pro Ile Cys
1 5

<210> 145
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 145

Cys Asp Asp Arg Thr Thr Lys Ile Cys
1 5

<210> 146

<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 146

Cys Trp Trp Pro Asp Gly Trp Tyr Cys
1 5

<210> 147
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 147

Cys Lys Leu Gln Leu Thr Asn Gln Cys
1 5

<210> 148
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 148

Cys Trp His Gly Leu Gly Gly Asn Cys
1 5

<210> 149
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 149

Cys His Ile Thr Leu Leu Lys Arg Cys
1 5

<210> 150
<211> 9

<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 150

Cys Glu Ser Met Ala Arg Pro His Cys
1 5

<210> 151
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 151

Cys His Trp Ser Trp Trp His Pro Cys
1 5

<210> 152
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 152

Cys Thr Leu Leu Leu Ser Arg Asn Cys
1 5

<210> 153
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 153

Cys Ser Ser Val Ser Tyr Met Ala Cys
1 5

<210> 154
<211> 9
<212> PRT

<213> artificial sequence

<220>
<223> peptide

<400> 154

Cys His Trp Arg Trp Leu Pro Ala Cys
1 5

<210> 155
<211> 11
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 155

Trp Ser Pro Gly Gln Gln Arg Leu His Asn Ser Xaa
1 5 10

<210> 156
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<220>
<221> misc_feature
<222> (12)..(12)
<223> X = any amino acid

<400> 156

Asp Ser Ser Asn Pro Ile Phe Trp Arg Pro Ser Ser
1 5 10

<210> 157
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 157

Glu Pro Phe Pro Ala Ser Ser Leu Met Thr Ile Arg
1 5 10

<210> 158
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 158

Ser Tyr His Trp Asp Lys Thr Pro Gln Val Leu Ile
1 5 10

<210> 159
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 159

Ser Gly His Gln Leu Leu Leu Asn Lys Met Pro Asn
1 5 10

<210> 160
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 160

Ser Ile Pro Ser Glu Ala Ser Leu Ser Ser Pro Arg
1 5 10

<210> 161
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 161

Thr Val Pro Pro Gln Leu Asn Ala Gln Phe Arg Ser
1 5 10

<210> 162
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 162

Ser Asp Asn Val His Thr Trp Gln Ala Met Phe Lys
1 5 10

<210> 163
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 163

Tyr Pro Ser Leu Leu Lys Met Gln Pro Gln Phe Ser
1 5 10

<210> 164
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 164

Leu Pro Ile Pro Ala His Val Ala Pro His Gly Pro
1 5 10

<210> 165
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 165

Leu Trp Gly Arg Pro Phe Pro Asp Leu Leu His Gln
1 5 10

<210> 166

<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 166

Gln Thr Pro Pro Trp Ile Leu Ser His Pro Pro Gln
1 5 10

<210> 167
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 167

Asn His Pro His Pro Thr Pro Ala Arg Gly Ile Ile
1 5 10

<210> 168
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 168

His Pro Ser Ser Ala Pro Trp Gly Val Ala Leu Ala
1 5 10

<210> 169
<211> 11
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 169

His Trp Asn His Arg Tyr Ser Met Trp Gly Ala
1 5 10

<210> 170
<211> 12

<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 170

Asn His Arg Ile Trp Glu Ser Phe Trp Pro Ser Ala
1 5 10

<210> 171
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 171

His Ser Ser Trp Trp Leu Ala Leu Ala Lys Pro Thr
1 5 10

<210> 172
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 172

Ser Asn Asn Asp Leu Ser Pro Leu Gln Thr Ser His
1 5 10

<210> 173
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 173

Ser Gly Leu Pro His Leu Ser Leu Asn Ala Pro Arg
1 5 10

<210> 174
<211> 12
<212> PRT

<213> artificial sequence

<220>
<223> peptide

<400> 174

Ser Trp Pro Leu Tyr Ser Arg Asp Ser Gly Leu Gly
1 5 10

<210> 175
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 175

Leu Pro Gly Trp Pro Leu Ala Glu Arg Val Gly Gln
1 5 10

<210> 176
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 176

Ser His Pro Trp Asn Ala Gln Arg Glu Leu Ser Val
1 5 10

<210> 177
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 177

Val Ser Arg His Gln Ser Trp His Pro His Asp Leu
1 5 10

<210> 178
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 178

Tyr Trp Pro Ser Lys His Trp Trp Trp Leu Ala Pro
1 5 10

<210> 179
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 179

Ser Ser Ala Trp Trp Ser Tyr Trp Pro Pro Val Ala
1 5 10

<210> 180
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 180

Ala Pro Leu Gly Phe Asn Ser Met Arg Leu Pro Ala
1 5 10

<210> 181
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 181

Trp Asn Met Arg Trp Leu Pro Thr Trp Ala Pro Ala
1 5 10

<210> 182
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 182

Trp Pro Arg Tyr Pro Ser Thr Leu Val Ser Ser His
1 5 10

<210> 183
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 183

Gly Lys Glu Ser Val Pro Pro Pro Arg Ile Tyr Ala
1 5 10

<210> 184
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 184

Leu Thr Leu Asp Met Lys Arg Thr Ser Gly Pro Leu
1 5 10

<210> 185
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 185

Leu Ser Thr His Thr Thr Glu Ser Arg Ser Met Val
1 5 10

<210> 186
<211> 12
<212> PRT
<213> artificial sequence

<220>

<223> peptide

<400> 186

Glu Tyr Leu Ser Ala Ile Val Ala Gly Pro Trp Pro
1 5 10

<210> 187
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 187

Gln Phe Lys Trp Trp His Ser Leu Ser Pro Thr Pro
1 5 10

<210> 188
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 188

Ala Pro Thr Pro Leu Ile Gly Lys Arg Leu Val Gln
1 5 10

<210> 189
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 189

Leu Ile Asn Pro Arg Asp His Val Leu Ala Pro Gln
1 5 10

<210> 190
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 190

Leu Leu Ala Asp Thr Thr His His Arg Pro Trp Thr
1 5 10

<210> 191
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 191

Gln Ala Ser Ile Ser Pro Leu Trp Thr Pro Thr Pro
1 5 10

<210> 192
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<220>
<221> misc_feature
<222> (3)..(3)
<223> X = any amino acid

<400> 192

Asn Ser Xaa Leu His Leu Ala His Gln Pro His Lys
1 5 10

<210> 193
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 193

Thr Lys Asn Met Leu Ser Leu Pro Val Gly Pro Gly
1 5 10

<210> 194
<211> 12

<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 194

Asp Met Pro Arg Thr Thr Met Ser Pro Pro Pro Arg
1 5 10

<210> 195
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 195

Ser Thr Pro Ala Leu Met Thr Leu Ile Ala Arg Thr
1 5 10

<210> 196
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 196

Thr Ser Asn Phe Ile Asn Arg Met Asn Pro Gly Leu
1 5 10

<210> 197
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 197

Thr Ser Ala Ser Thr Arg Pro Glu Leu His Tyr Pro
1 5 10

<210> 198
<211> 12
<212> PRT

<213> artificial sequence

<220>
<223> peptide

<400> 198

Asn Leu Leu Glu Val Ile Ser Leu Pro His Arg Gly
1 5 10

<210> 199
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 199

Gln His Pro Asn Asn Ala His Val Arg Gln Phe Pro
1 5 10

<210> 200
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 200

Gln His Ala Asn Asn Gln Ala Trp Asn Asn Leu Arg
1 5 10

<210> 201
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 201

Gln His Tyr Pro Gly Arg Ala Ile Pro His Ser Thr
1 5 10

<210> 202
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 202

Val Pro Pro Pro His Pro Gln Phe Asp His Leu Ile
1 5 10

<210> 203
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 203

Leu Lys Met Asn Pro Ser Ile Ser Ser Ser Leu Lys
1 5 10

<210> 204
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 204

His Trp Asp Pro Phe Ser Leu Ser Ala Tyr Phe Pro
1 5 10

<210> 205
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 205

Trp Ser Pro Gly Gln Gln Arg Leu His Asn Ser Thr
1 5 10

<210> 206
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 206

Asn Met Thr Lys His Pro Leu Ala Tyr Thr Glu Pro
1 5 10

<210> 207
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 207

His Met Pro Thr Lys Ser Ala Ser Gln Thr Tyr Phe
1 5 10

<210> 208
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 208

His Asn Ala Tyr Trp His Trp Pro Pro Ser Met Thr
1 5 10

<210> 209
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 209

Val Leu Pro Pro Lys Pro Met Arg Gln Pro Val Ala
1 5 10

<210> 210
<211> 12
<212> PRT
<213> artificial sequence

<220>

<223> peptide

<400> 210

Ser Leu His Lys Ile Ser Gln Leu Ser Phe Ala Ser
1 5 10

<210> 211
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 211

Trp His Ser Arg Leu Pro Pro Met Thr Val Ala Phe
1 5 10

<210> 212
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 212

Thr Pro Trp Phe Gln Trp His Gln Trp Asn Leu Asn
1 5 10

<210> 213
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 213

Ser Asp Thr Ile Ser Arg Leu His Val Ser Met Thr
1 5 10

<210> 214
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 214

Asn Pro Tyr His Pro Thr Ile Pro Gln Ser Val His
1 5 10

<210> 215
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 215

Leu Pro Ser Ala Lys Leu Pro Pro Gly Pro Pro Lys
1 5 10

<210> 216
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 216

Thr Ser Asn Pro His Thr Arg His Tyr Tyr Pro Ile
1 5 10

<210> 217
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 217

Ser Asn Phe Thr Thr Gln Met Thr Phe Tyr Thr Gly
1 5 10

<210> 218
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 218

Lys Met Asp Arg His Asp Pro Ser Pro Ala Leu Leu
1 5 10

<210> 219
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 219

Met Pro Ala Val Met Ser Ser Ala Gln Val Pro Arg
1 5 10

<210> 220
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 220

Asp Arg Ala Pro Leu Ile Pro Phe Ala Ser Gln His
1 5 10

<210> 221
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 221

Asp Gln Tyr Ile Gln Gln Ala His Arg Ser His Ile
1 5 10

<210> 222
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 222

His Ala Arg Ile Asn Pro Ser Phe Pro Leu Pro Ile
1 5 10

<210> 223
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 223

Gly Trp Trp Pro Tyr Ala Ala Leu Arg Ala Leu Ser
1 5 10

<210> 224
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 224

Thr Ala Ala Thr Ser Ser Pro His Ser Arg Ser Pro
1 5 10

<210> 225
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 225

Ser Thr Thr Gly Gln Ser Pro Ala Leu Ala Pro Pro
1 5 10

<210> 226
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 226

His Ser Ser Trp Tyr Ile Gln His Phe Pro Pro Leu
1 5 10

<210> 227
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 227

Gly Ser His Ser Asn Pro Thr Pro Leu Thr Pro Arg
1 5 10

<210> 228
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 228

Tyr Thr Gly Val Leu Asp Thr Lys Ala Thr Gln Asn
1 5 10

<210> 229
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 229

Asn Asn Pro His Met Gln Asn
1 5

<210> 230
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 230

Val Ile Ser Asn His Ala Glu Ser Ser Arg Arg Leu

1 5 10

<210> 231
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 231

Asp Ser Pro His Arg His Ser
1 5

<210> 232
<211> 8
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 232

Asn Asn Pro Met His Gln Asn Cys
1 5

<210> 233
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 233

Ser Gly Pro Ala His Gly Met Phe Ala Arg
1 5 10

<210> 234
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 234

Cys Thr Tyr Ser Arg Leu His Leu Cys
1 5

<210> 235
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 235

Cys Arg Pro Tyr Asn Ile His Gln Cys
1 5

<210> 236
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 236

Cys Pro Phe Lys Thr Ala Phe Pro Cys
1 5

<210> 237
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<220>
<221> misc_feature
<222> (1)..(2)
<223> X = N or Q

<220>
<221> misc_feature
<222> (6)..(7)
<223> X = N or Q

<400> 237

Xaa Xaa Pro Met His Xaa Xaa
1 5

<210> 238

<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 238

Trp Trp Ser Trp His Pro Trp
1 5

<210> 239
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 239

His Trp Ser Trp Trp His Pro
1 5

<210> 240
<211> 14
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 240

Ala Cys Trp Trp Ser Trp His Pro Trp Cys Gly Gly Gly Lys
1 5 10

<210> 241
<211> 14
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 241

Ala Cys Asp Ser Pro His Arg His Ser Cys Gly Gly Gly Lys
1 5 10

<210> 242
<211> 14

<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 242

Ala Cys Pro Arg Ser Ser His Asp His Cys Gly Gly Gly Lys
1 5 10

<210> 243
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 243

Tyr Phe Ser Trp Trp His Pro
1 5

<210> 244
<211> 16
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 244

Asp Met Pro Arg Thr Thr Met Ser Pro Pro Pro Arg Gly Gly Gly Lys
1 5 10 15

<210> 245
<211> 12
<212> PRT
<213> artificial sequence

<220>
<223> peptide

<400> 245

Asn His Arg Ile Trp Glu Ser Phe Trp Pro Ser Ala
1 5 10

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 April 2003 (03.04.2003)

PCT

(10) International Publication Number
WO 03/026590 A3

(51) International Patent Classification[7]: B05D 3/10, 7/02, B32B 5/16, G01N 1/36, 21/63, G01J 5/02, C12Q 1/68, 1/00, C07H 17/00, 19/00

(21) International Application Number: PCT/US02/31091

(22) International Filing Date:
27 September 2002 (27.09.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/325,664 28 September 2001 (28.09.2001) US

(71) Applicant: **BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM** [US/US]; 201 West 7th Street, Austin, TX 78701 (US).

(72) Inventors: **BELCHER, Angela, M.**; 35 Balfour Street, Lexington, MA 02421 (US). **SMALLEY, Richard, E.**; Rice University, Space Science Bldg, Room 301a, 6100 Main Street, Houston, TX 77005-1892 (US). **RYAN, Esther**; 11653 Cherryview Lane, San Jose, CA 95116 (US). **LEE, Seung-Wuk**; Rice University, Space Science Bldg, Room 301a, 6100 Main Street, Houston, TX 77005-1892 (US).

(74) Agents: **WARREN, Sanford, E., Jr.** et al.; Gardere Wynne Sewell LLP, Suite 3000, 1601 Elm Street, Dallas, TX 75201-4761 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
4 December 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/026590 A3

(54) Title: BIOLOGICAL CONTROL OF NANOPARTICLES

(57) Abstract: The present invention includes compositions and methods for selective binding of amino acid oligomers to semiconductor and elemental carbon-containing materials. One form of the present invention is a method for controlling the particle size of the semiconductor or elemental carbon-containing material by interacting an amino acid oligomer that specifically binds the material with solutions that can result in the formation of the material. The same method can be used to control the aspect ratio of the nanocrystal particles of the semiconductor material. Another form of the present invention is a method to create nanowires from the semiconductor or elemental carbon-containing material. Yet another form of the present invention is a biologic scaffold comprising a substrate capable of binding one or more biologic materials, one or more biologic materials attached to the substrate, and one or more elemental carbon-containing molecules attached to one or more biologic materials.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/31091

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : B05D 3/10, 7/02; B32B 5/16; G01N 1/36, 21/63; G01J 5/02; C12Q 1/68, 1/00; C07H 17/00, 19/00
US CL : 435/6, 7.1, 7.37; 536/24.3, 23.1; 530/391.1; 250/307; 427/2.13; 428/323

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6, 7.1, 7.37; 536/24.3, 23.1; 530/391.1; 250/307; 427/2.13; 428/323

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,990,479 A (WEISS et al.) 23 November 1999 (23.11.1999), entire document.	49-50, 96-103, and 106
---		---
Y		1-59, 62-72, 75-79, 81-92, 94-103, 106-113
X	US 5,985,353 A (LAWTON et al.) 16 November 1999 (16.11.1999), entire document.	35-41, 49-50, 96-103, and 106
---		---
Y		1-59, 62-72, 75-79, 81-92, 94-103, 106-113
Y	US 6,207,392 B1 (WEISS et al.) 27 March 2001 (27.03.2001), entire document.	1-41, 49-50, 96-103, and 106
Y	WO 99/13313 A1 (GENOVATIONS, INC.) 18 March 1999 (18.03.1999), entire document.	1-51, 96-103, and 106
Y,P	WO 02/48701 A2 (PRESIDENT AND FELLOWS OF HARVARD COLLEGE 20 June 2002 (20.06.2002), entire document.	1-52, 96-103, and 106

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
11 March 2003 (11.03.2003)

Date of mailing of the international search report
18 APR 2003

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703)305-3230

Authorized officer
My-Chau T. Tran

Telephone No. 703-308-1123

Form PCT/ISA/210 (second sheet) (July 1998)

PCT/US02/31091

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	WO 91/14696 A1 (GILEAD SCIENCES, INC.) 03 October 1991 (03.10.91), entire document.	52-59, 62-72. 75-79, 81-90, 92, 94-103, and 106 --- 107-112
X --- Y	US 5,270,170 A (SCHATZ et al.) 14 December 1993 (14.12.1993), entire document.	52-59, 62-72. 75-79, 81-90, 92, 94-103, and 106 --- 107-112
X	US 5,739,305 A (CUBICCIOTI) 14 April 1998 (14.04.1998), entire document.	52-59, 62-72. 75-79, 81-90, 92, 94-103, and 106-112
Y	US 5,510,240 A (LAM et al.) 23 April 1996 (23.04.1996), entire document.	52-59, 62-72. 75-79, 81-90, 92, 94-103, and 106-112
Y	US 5,683,867 A (BIESECKER et al.) 04 November 1997 (04.11.1997), entire document.	52-59, 62-72. 75-79, 81-90, 92, 94-103, and 106-112
Y	US 5,714,330 A (BRENNER et al.) 03 February 1998 (03.02.1998), entire document.	52-59, 62-72. 75-79, 81-90, 92, 94-103, and 106-112
Y	US 5,859,210 A (STOWOLITZ et al.) 12 January 1999 (12.01.1999), entire document.	52-59, 62-72. 75-79, 81-90, 92, 94-103, and 106-112

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/31091

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claim Nos.: 60,61,73,74,80,91,93,104 and 105
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claims 60-61, 73-74, 80, 91, 93, and 104-105 are unsearchable because no computer readable forms of the sequence listings are furnished.

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.